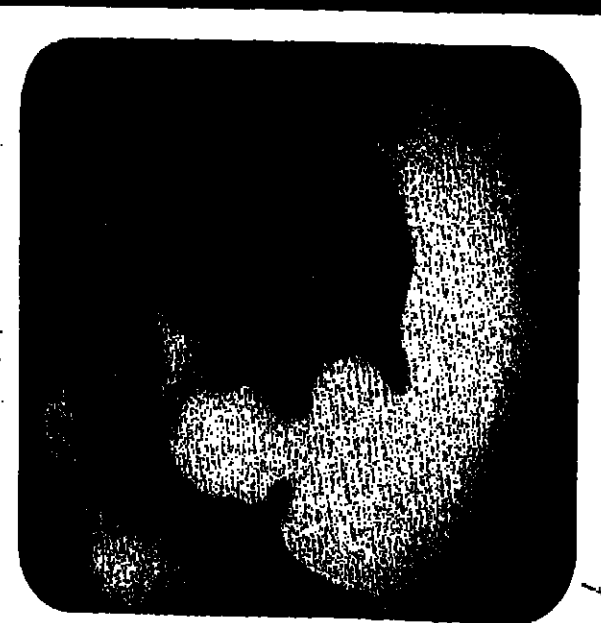


The Upper Functional G.I. Disorder

The Pseudo-ulcer



Ulcer-like symptoms: no G.I. pathology

The patient is convinced it's an ulcer. However, symptoms are not quite typical, and x-ray findings are negative. These findings and the results of additional diagnostic procedures exclude an organic basis for the patient's complaints. A diagnosis of "upper functional gastrointestinal disorder" is made, which is supported by the fact that episodes of painful symptoms coincide with episodes of excessive anxiety, as indicated by the history.

It may be useful to explain to the patient the mechanism by which emotions upset normal G.I. functioning, resulting in hypersecretion and hypermotility and thus causing such symptoms as nausea and epigastric pain. In upper functional gastrointestinal disorders, counseling by the primary physician can often help the patient to understand how excessive anxiety may cause flare-ups of G.I. symptoms.

A disproportionate number of patients seen by the general practitioner suffer from functional disorders, as do more than half of those seen by the gastroenterologist. Where milder cases may respond to counsel-

ing alone, if symptoms are severe and disabling to any degree, a suitable regimen may include medication to reduce the symptoms and the excessive anxiety that often provokes these distressing symptoms.

In these cases, Librax as an adjunct can greatly contribute to the course of therapy. Its dual action can offer relief of both painful symptoms and excessive anxiety, because each capsule contains 5 mg chlorthalidone HCl and 2.5 mg clidinium Br. The antianxiety action of Librax® (chlorthalidone HCl) makes Librax exceptional

An adjunct
in anxiety-related upper
functional G.I. disorders

Librax®

Each capsule contains 5 mg chlorthalidone HCl and 2.5 mg clidinium Br.

among drugs for certain gastrointestinal disorders associated with excessive anxiety; the clidinium bromide (Quarzan®) component furnishes dependable antispasmodic action. Dosage is flexible; it may be adjusted according to your patient's requirements within the range of 1 or 2 capsules three or four times daily, up to 8 capsules daily in divided doses.

*Rome HP, Brannick TL: Orientation and mechanism of functional disorders: clinical pharmacology correlation, chap. 188, in *Gastroenterology*, edited by Bockus HJ. Philadelphia, WB Saunders Company, 1965, p. 1118

pregnancy, lactation, or in women of childbearing age requires that its potential benefits be weighed against its possible hazards. As with all anticholinergic drugs, an inhibiting effect on lactation may occur.

Precautions In elderly and debilitated, limit dosage to smallest effective amount to preclude development of ataxia, overexcitation or confusion (not more than two capsules per day initially, increase gradually as needed and tolerated). Though generally not recommended, if combination therapy with other psychotropics seems indicated, carefully consider individual pharmacologic effects, particularly in use of potent drugs such as MAO inhibitors and phenothiazines. Observe usual precautions in presence of impaired renal or hepatic function. Paradoxical reactions (e.g., excitement, stimulation and acute rage) have been reported in psychiatric patients. Employ usual precautions in treatment of anxiety states with evidence of impending depression. Variable effects on blood coagulation have been reported. Variable in patients receiving the drug and oral anticoagulants; causal relationship has not been established clinically.

Adverse Reactions No side effects or manifestations not seen with either compound alone have been reported with Librax. When chlorthalidone hydrochloride is used alone, drowsi-

ness, ataxia and confusion may occur, especially in the elderly and debilitated. These are reversible in most instances by proper dosage adjustment; but are also occasionally observed at the lower dosage ranges. In a few instances syncope has been reported. Also encountered are isolated instances of skin eruptions, edema, minor menstrual irregularities, nausea and constipation, extrapyramidal symptoms, increased and decreased libido—all infrequent and generally controlled with dosage reduction; changes in EEG patterns (low-voltage, dysrhythmia) may appear during and after treatment; blood dyscrasias (including agranulocytosis), jaundice and hepatic dysfunction have been reported occasionally with chlorthalidone hydrochloride, making periodic blood counts and liver function tests advisable during protracted therapy. Adverse effects reported with Librax are typical of anticholinergic agents, i.e., dryness of mouth, blurring of vision, urinary hesitancy and constipation. Constipation has occurred most often when Librax therapy is combined with other spasmolytics and/or low residue diets.

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Division of Hoffmann-La Roche Inc.
Nutley, New Jersey 07110

Before prescribing, please consult complete product information, a summary of which follows:

Indications Symptomatic relief of hypersecretion, hypermotility and anxiety and tension states associated with organic or functional gastrointestinal disorders; and as adjunctive therapy in the management of peptic ulcer, gastric duodenal, irritable bowel syndrome, gastric colitis, and mild vesicular colitis.

Contraindications Patients with glaucoma; prostatic hypertrophy and benign bladder neck obstruction; known hypersensitivity to chlorthalidone hydrochloride and/or clidinium bromide.

Warnings Caution patients about possible combined effects with alcohol and other CNS depressants. As with all CNS-acting drugs, caution patients against hazardous occupations requiring complete mental alertness (e.g., operating machinery, driving). Though physical and psychological dependence have rarely been reported on recommended doses, use caution in administering Librax to individuals or those who might increase dosage without medical supervision (including convulsions following discontinuation of the drug and similar to those seen with barbiturates, have been reported. Use of any drug in

Good Trib 14
GOOD DRUGS DO
the therapeutic winning team supplement
dedicated to the physician-patient relationship

Medical Tribune

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Vol. 17, No. 14

world news of medicine and its practice—fast, accurate, complete

and Medical News

Wednesday, April 14, 1976

Oral Zinc Said To Ease Pain Of Sickle Cell

By MICHAEL HERRING
Medical Tribune Staff

ANN ARBOR, MICH.—High daily doses of oral zinc acetate appear to prevent and relieve pain crises in sickle cell anemia patients, researchers here and in Detroit have announced.

The metal, unknown as a human trace element as late as 1962, has been shown to lower the number of irreversibly sickled cells (ISCs) in at least four patients, the researchers indicated.

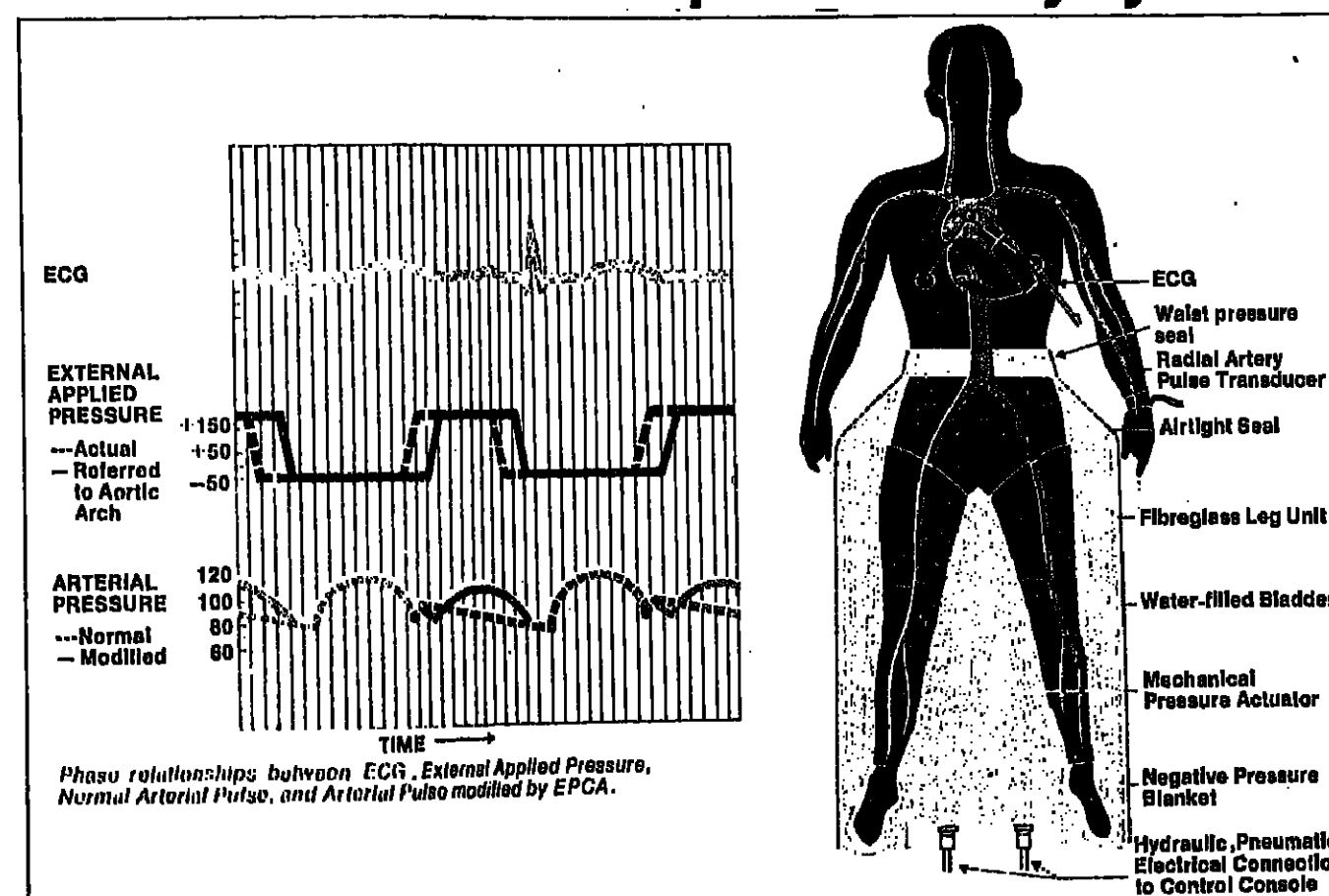
Drs. George E. Brewer, Professor of Human Genetics at the University of Michigan, and Ananda Prasad, Professor of Medicine and Director of the Division of Hematology at Wayne State University, are collaborating on a controlled, double-blind, crossover study of about 10 sickle-cell patients to confirm these findings.

"Uncontrolled data have already indicated that zinc has a beneficial effect in pain crises. Now we want to weed out the placebo effect," Dr. Prasad said in an interview with MEDICAL TRIBUNE.

The controlled study, he added, will include patients from his and Dr. Brewer's clinics. Half the patients will be given the oral zinc acetate, the other half placebo. At the end of six months, Continued on page 23

25-Center Collaborative Study Finds:

EPCA Cuts Acute MI Inhospital Mortality by 50%



Phase relationships between ECG, External Applied Pressure, Normal Arterial Pulse, and Arterial Pulse modified by EPCA.

EPCA entails encasing the legs in a trouser-like device, right, and alternately applying positive and negative pressure to the vascular bed. Pressures are synchronized through signals from ECG leads and phased to produce positive pressure during diastole and negative pressure during systole. Controlled aortic pressure reduces heart work and increases coronary arterial flow. Phase relationships between ECG, external applied pressure, normal arterial pulse, and EPCA-modified pulse are shown at left. (Graphics courtesy of Medical Innovations, Inc.)

By NATHAN HORWITZ
Medical Tribune Staff

NEW ORLEANS—A collaborative study at 25 centers across the nation suggests that external pressure circulatory assist (EPCA) reduces hospital mortality by more than 50% in patients with acute myocardial infarction.

In addition, the findings have shown that fewer than 1% of EPCA-treated patients experienced ventricular fibrillation, compared to 7% of controls, and "significantly fewer" of the treated

group underwent a worsening of clinical status, the American College of Cardiology was told here by Dr. Ezra A. Amsterdam, Associate Professor of Medicine, University of California School of Medicine at Davis.

The results suggest that "the routine early use of EPCA may be warranted, especially in uncomplicated or mild acute myocardial infarction," Dr. Amsterdam declared.

The prospective national trial of Continued on page 29

Blood ACTH Assay Termed 'Premature' as Ca Screen

By FRANCES GOODNIGHT
Medical Tribune Staff

NEW YORK—It is "premature" now to think that examination of blood samples for elevated levels of ACTH can be used as a mass screening procedure to detect early lung cancer—even though the finding of the hormone in long cancer tissue suggests that blood concentrations may prove a biologic marker.

This caution was sounded here by Rosalyn S. Yalow, Ph.D., co-developer of the radioimmunoassay technique and the scientist whose investigations at

ACTH in lung cancer tissue first sparked hopes that the malignancy might be detected solely by blood screening.

Dr. Yalow, senior medical investigator at the Solomon A. Berson Research Laboratory, Bronx (N.Y.) Veterans Administration Hospital, reported that both false positives and false negatives had been observed in studies conducted so far on plasma levels of the hormone in patients with and without lung cancer.

The central questions that must be Continued on page 8

Proceeding Cautiously Anti-Pregnancy Subunit Vaccine In Clinical Tests

Medical Tribune Report

NEW YORK—A vaccine that may make it possible to immunize against pregnancy has been developed by investigators at the All India Institute of Medical Sciences, New Delhi, and is now undergoing both confirmatory testing in subhuman primates and cautious clinical trials at research centers in other countries.

The immunizing compound is a conjugate of the "processed" beta-subunit of human chorionic gonadotropin (HCG) plus tetanus toxoid in the role of co-antigen, according to Dr. G. P. Talwar, who heads the Indian team.

The goal is to inactivate by means of circulating antibodies the HCG that is produced by trophoblasts within the first week after fertilization and that is crucial to maintenance of pregnancy.

Extensive tests have been conducted by Dr. Talwar and colleagues at the institute on several animal species, and Continued on page 21

An open letter to the doctors of America

Subject: The all-important physician-patient relationship

Dear Doctor:

We must and will do something about it.

The science and art of medicine has reached its most advanced state but the all-important physician-patient relationship is plunging to an all-time low.

We must do something about it.

The establishment of "cost-effective" control rather than "therapeutic-effective" practice is part of the drive towards the government's dominance, if not takeover, of medicine. Physicians personally, and the medical profession generally; medicines specifically, and diagnostic and other procedures generally, have become a target for governmental attacks as a result of the pressures generated through sensation-seeking consumerism and political expediency.

Patient regimens are too often disrupted, medical advice disregarded and medications neglected. Early diagnosis of essential conditions is being placed in jeopardy and early treatment delayed.

We must do something about it.

Medical Tribune has addressed these issues editorially. Medical Tribune has encouraged the mobilization of official bodies of medicine. It has reported extensively on constructive efforts by *ad hoc* committees of physicians. We have discussed these problems at great length with responsible consumer leaders, leaders in all fields of medicine, and with a whole gamut of government officials.

More is needed.

Medical Tribune has developed and is introducing an innovation in patient education to help rebuild and sustain the all-important physician-patient relationship. Medical Tribune has prepared a series of supplements

for use in physicians' waiting rooms, clinics, and hospitals, entitled THE GOOD DRUGS DO. Each supplement is prepared by an outstanding leader in one of the fields of medicine. Each supplement is written so that the patient can understand it. Each seeks to advance the goal of an informed patient, a cooperative patient, and a patient confident in his physician's practices, medicines and recommendations. The waiting room patient supplement, THE GOOD DRUGS DO, will be coming to you as a section of Medical Tribune.

THE GOOD DRUGS DO patient supplement in Medical Tribune seeks to do something positive about the physician-patient relationship.

THE GOOD DRUGS DO supplements prepared thus far consist of a general introduction by Dr. Louis Lasagna, covering the broad advance made by therapeutic medicine in the Golden Age of Therapeutics, THE GOOD DRUGS DO individual supplements then go on to take up Depression, Hypertension, Nutrition and Vitamins, Alcoholism, Diabetes, Arthritis, Psychoses, Antibiotics. Each subject supplement is prepared by an outstanding authority in the field and addressed to patients.

Please remove THE GOOD DRUGS DO supplements from coming issues of Medical Tribune and put them in your waiting room.

You can help us help your patients by making this essential material available to them and by advising us as to how we may make improvements in your and your patients' interests.

We can do something about the all-important physician-patient relationship.

Sincerely,

Arthur M. Sackler
International Publisher

Primary Lung Ca Survival Tied to Early Diagnosis

Medical Tribune Report

SAN ANTONIO, TEX.—Evidence that survival in primary lung cancer is dependent upon early diagnosis has been provided by the records of 3,000 patients entered in the Armed Forces Central Medical Registry, a team of Air Force investigators reported here.

Citing overall figures, Col. William Stanford (USAF, MC), of Wilford Hall USAF Medical Center, Lackland (Texas) Air Force Base, said that only 18.2% of the 3,000 patients were alive at five years and 14.5% at 10 years.

In sharp contrast, the five-year survival was 48.8%, and the 10-year rate was 38.6%, among the 1,027 patients in whom definitive surgery (for cure, as opposed to palliation) could be carried out and all identifiable tumor removed. If nodal involvement was found in the specimen, however, the five-year survival rate dropped to 30%.

Select Group

Factors affecting the improved outlook seen in the CMR population as compared to some civilian groups "appear to be related to a ready accessibility of medical care, and the necessity—because of global commitments—of establishing an early diagnosis," Dr. Stanford told an Air Force Regional Meeting of the American College of Physicians.

The registry at Brooks Air Force Base, Texas, he pointed out, receives records from military hospitals located in all parts of the world. Thus, he considers the 3,000 patients "a select group," since they can obtain care promptly without added expense, and have periodic physical examinations as well as frequent chest x-rays.

Workups of such patients often include brain and bone scans, bronchoscopy, cervical mediastinal exploration, and other tests, he added.

"These factors are probably reflected in the fact that 71.1% of our patients had no organ metastases when first seen, and that over 50% of the series had no evidence of lymph node involvement," he said.

Data from the records analysis also indicate, Dr. Stanford believes, that the major determinants of survival are the presence or absence of lymph node metastases rather than tumor cell type.

As expected, the prognosis for patients with either squamous cell carcinoma or adenocarcinoma was better than for those with tumors categorized as small cell, large cell, oat cell, and undifferentiated cell types.

In squamous cell and adenocarcinoma patients who could be treated with definitive resection, the five-year survival was 47.6% and 50.8%.

Overall survival rates following palliative surgery, palliative radiation, or chemotherapy (received at any point postdiagnosis) were below 5%.

Coauthors of the report were Drs. Gordon L. Larsen and James A. Alexander, of Wilford Hall USAF Medical Center, and Dr. Charles G. Spivey and William J. Besich of the Armed Forces Central Medical Registry.

Routine Postop Anticoagulant In Hip Fractures Challenged

By ANASTASIA TOUFEXIS
Medical Tribune Staff

NEW ORLEANS—The routine use of anticoagulants to prevent thromboembolic complications in postoperative management of patients with hip fractures and total hip replacements was challenged at a meeting here of the American Academy of Orthopaedic Surgeons.

In a paper on thromboembolic complications in hip fracture, labeled "controversial" by many, Dr. Lorraine Day argued that the scope of the problem is as yet unknown ("How high is the incidence of pulmonary embolism?") and that early mobilization of patients following surgery might be as effective as and even safer than anticoagulation in preventing formation of pulmonary emboli. Dr. Day is Assistant Professor of Orthopaedic Surgery at the University of California, San Francisco.

Get Patients Up

Dr. Day disagrees with the theory that pulmonary embolism is a daily problem on orthopedic wards. "The point I'm trying to refute," she told MEDICAL TRIBUNE, "is that pulmonary embolism happens so frequently that prophylaxis with drugs is necessary. The word from some areas is that there are so many cases of pulmonary embolism in hip fracture that we must do something to prevent it. What we do here is get patients out of bed right away. That's our prophylaxis."

Although her paper dealt with hip fractures, Dr. Day indicated in the interview that her views extend to total hip replacements as well.

She believes that pulmonary embolism may well be overdiagnosed, rather than underdiagnosed as many authors suggest. She points out that a diagnosis of pulmonary embolism, despite lung scans and pulmonary arteriograms, is difficult to make. "In two cases reviewed at our hospital, the patient was given the clinical diagnosis of pulmonary embolism, when the autopsy showed death was caused by acute aspiration," she noted.

New Imaging System Cuts Radiation Dose

Medical Tribune Report

LAS VEGAS, NEV.—A new mammography system which uses reduced radiation dosages in imaging the breast for cancer screening was demonstrated here at the 15th annual Conference on Detection and Treatment of Early Breast Cancer.

The new system, called Lo-dose/2 and manufactured by the DuPont Company, requires 50% less patient exposure than standard mammography.

Clinical evaluations over the past six months at Albert Einstein Medical Center in Philadelphia, the University of Michigan, the University of California-Los Angeles, and New York's Memorial Sloan-Kettering Cancer Center, indicate the new Lo-dose/2 image to be completely diagnostic, a DuPont spokesman said.

Dr. Day also pointed out that "once the clinical diagnosis of pulmonary embolism is made, it follows the patient indefinitely and he is subjected to the hazards of anticoagulant therapy with every subsequent episode of bed rest or surgery."

"We just don't have a baseline on the incidence of pulmonary embolism to judge whether giving potentially hazardous anticoagulants is necessary," she told MEDICAL TRIBUNE. "We need controlled studies with autopsies of all deaths."

Furthermore, said Dr. Day, "We have to make sure the drug isn't worse than the disease." An analysis of data showed that the mortality rate from pulmonary embolism in patients not receiving anticoagulant prophylaxis was lower than mortality rates from hemorrhagic complications reported by others who used heparin in attempts to prevent pulmonary embolism, according to Dr. Day.

"Our mortality rate from pulmonary embolism in hip fractures without prophylaxis is less than 1%," she said. "Fatal hemorrhagic complications from anticoagulation can approach 2%." With a mortality rate as low as we have reported, the prophylactic use of any drug with significant side effects is unwarranted.

The 2% figure was disputed by Dr. William D. Arnold, director of the combined fracture service of New York Hospital and the Hospital for Special Surgery in New York City. "In terms of prophylactic anticoagulation, the death rate should be closer to zero, not 2%," Dr. Arnold told MEDICAL TRIBUNE.

He believes Dr. Day is confusing therapy with prophylaxis. "With the therapeutic use of heparin for established pulmonary emboli, it is possible that a number of complications due to anticoagulation therapy will be encountered, but this is not the same as prophylactic use of anticoagulation," he stressed.

Dr. Arnold advocates selective prophylactic anticoagulation in patients with hip fractures, "specifically those who require prolonged bed rest, have histories of thromboembolic disease, or are about to undergo prosthetic replacement."

However, he does routinely "and safely" anticoagulate patients in total hip replacements. "Several studies of total hip replacements shortly to be reported show no fatalities and no fatal pulmonary emboli following routine anticoagulation with low-dose heparin, dextran, aspirin or (sodium warfarin)," he said.

Dr. Day's conclusions were based on a review of 302 patients with hip fracture admitted to San Francisco General Hospital over a three-year period. Most (71%) of the patients were over age 55. "Our treatment for hip fracture during this time was early internal fixation (usually within one to seven days post injury) and mobilization the following day," she said. "No drug prophylaxis for thromboembolic complications was given and the patients did not wear special stockings."

'See the Pretty Baby'



To study development of body imagery in child, Dr. Taghi Modarressi, of U. of Maryland, holds up distorted mirror. Children begin to recognize image is wrong at 10-11 months. From 2-5 years of age, they believe image distortion equals distortion of self; 7 to 10-year-olds laugh and play before mirror. Results may suggest therapeutic approaches to emotional problems linked with self image.

Eighteen patients (6%) died in hospital and three more after discharge. All in-hospital deaths were autopsied. (Dr. Day pointed out that most incidence studies of pulmonary embolism have not autopsied all deaths which is the only way to verify the clinical diagnosis.)

"The total number of in-hospital deaths from pulmonary embolism was three patients out of 302 (less than 1%)," Dr. Day reported.

Studies from other centers show both higher mortality rates and a higher incidence of death from pulmonary embolism, according to Dr. Day. "I cannot explain why our mortality rate is much lower than the other series but one major factor may have been our attitude toward early mobilization," Dr. Day said. "Nearly all of our patients were out of bed the first or second postoperative day."

NIH Seeks Referrals Of Pituitary Tumors

Medical Tribune Report

BETHESDA, MD.—The cooperation of physicians is requested in the referral of patients with pituitary tumors (exclusive of those with acromegaly) for a study being conducted by branches of the National Institutes of Health.

A summary of the workup, findings, and disposition will be sent to the referring physician.

Physicians interested in having their patients considered for admission may contact: Dr. Charles A. Stott, NIH-NICHD Clinical Center, Room 10B-NICHD, Bethesda, Md. 20014; telephone: (301) 496-5909; or Dr. Ronald Kahn, NIH-NIAMDD Clinical Center, Room 8N-238, Bethesda, Md. 20014; telephone: (301) 496-2596.

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CLINICAL NEWS NOTE: "Only 25% of these [175 angina pectoris] patients [referred for angiography] had ever been told about the use of prophylactic nitroglycerin, and many of them who have been told, don't use it. So there's a two-way problem here—education by the physician and response by the patient." (Dr. Ezra A. Amsterdam. See page 12.)

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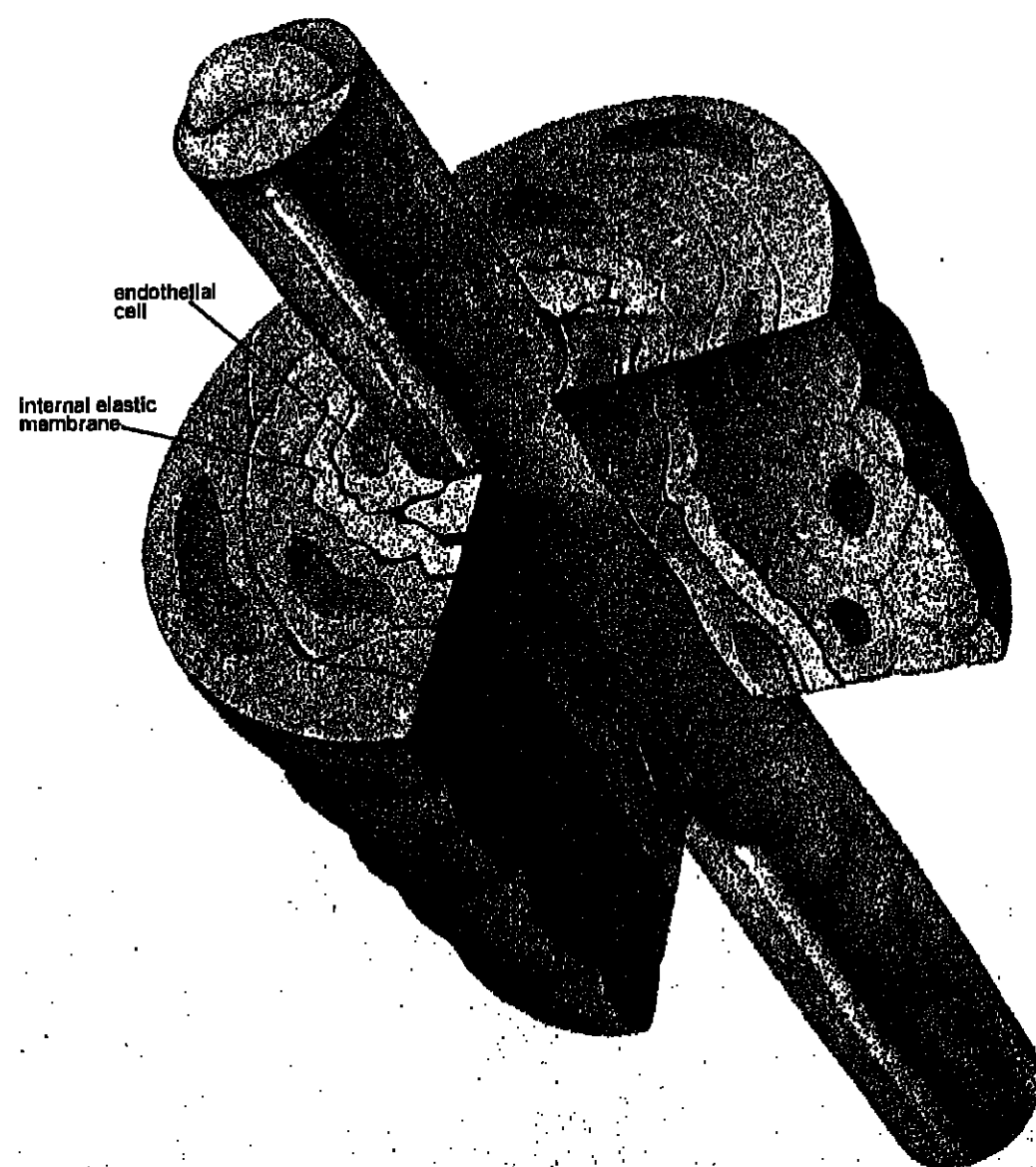
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Abnormally high peripheral resistance is the major hemodynamic problem with most hypertensives.

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high peripheral resistance: common attribute of most hypertensives

Because high peripheral resistance is the major hemodynamic disturbance found in most patients with essential hypertension,^{1,2} the therapeutic goal should be reduction of total peripheral resistance and a return to more normal peripheral circulation.^{1,2}

Hence, vasodilating drugs "...offer a physiologically rational approach to the therapy of hypertension." In addition, "...vasodilators [combined with a sympathetic inhibitor] are the most predictable and specific drugs for reversing the hemodynamic abnormality of most hypertensive patients."³

the only oral agent that deals directly with this problem

Apresoline (hydralazine), the only currently approved oral antihypertensive with vasodilating action, decreases peripheral resistance—regardless of its cause—and, hence, arterial pressure by relaxing arteriolar smooth muscle. Accompanying the fall in blood pressure is a rise in cardiac output and rate. Apresoline also maintains or increases renal and cerebral blood flow.

a different and complementary pharmacologic approach

Different in action from all other oral antihypertensives and compatible with most of them, Apresoline can play a significant role in a variety of therapeutic combinations.

Such combinations, according to Freis,⁴ with each component representing a different antihypertensive mecha-

nism, provide the most effective way to control blood pressure. This approach may also permit lower drug dosages.

the problem of postural hypotension minimized

Nickerson⁵ describes the action of Apresoline as follows:

"A preferential effect on arterioles, as compared to veins, allows the increase in cardiac output and minimizes postural hypotension; the latter is much less than that produced by agents blocking sympathetic nerves."

Continued on following page

Apresoline[®] hydrochloride (hydralazine hydrochloride)

TABLETS

INDICATIONS
Essential hypertension, alone or as an adjunct.

CONTRAINDICATIONS
Hypersensitivity; coronary artery disease; mitral valvular rheumatic heart disease.

WARNINGS
Hydralazine may produce in a few patients a clinical picture resembling systemic lupus erythematosus. In such patients hydralazine should be discontinued unless the benefit to risk determination requires continued antihypertensive therapy with

this drug. Symptoms and signs usually regress when the drug is discontinued but recrudescence has been detected many years later. Long-term treatment with steroids may be necessary.

PRECAUTIONS
Cardiac blood counts, L.E. cell preparations and chest x-rays should be obtained before and periodically during prolonged therapy even though patient is asymptomatic. These studies are also indicated in the presence of any unexplained symptoms.

A positive antinuclear antibody titer and/or positive L.E. cell reaction requires that the physician carefully weigh the implications of the test results against the benefits to be derived from antihypertensive therapy with hydralazine.

Use MAO inhibitors with caution.

Usage in Pregnancy
The drug should be used only when, in the judgment of the physician, it is deemed essential to the welfare of the patient.

PRECAUTIONS
Use cautiously in suspected coronary artery or other cardiovascular diseases, cerebral vascular accidents, and advanced renal damage. Postural hypotension may occur, and the pressor response to epinephrine may be reduced.

Peripheral neuritis, evidenced by paresthesias, numbness, and tingling, has been observed. Published evidence suggests an encephalopathy effect and addition of pyridoxine to the regimen if symptoms develop.

Blood dyscrasias, consisting of reduction in hemoglobin and red cell count, leukopenia, agranulocytosis, and purpura, have been reported rarely. If such abnormalities develop, discontinue

therapy. Periodic blood counts are advised during prolonged therapy.

ADVERSE REACTIONS

Common: Headache; palpitations; anorexia; nausea; vomiting; diarrhea; tachycardia; angina pectoris. Less frequent: nasal congestion; flushing; lacrimation; conjunctivitis; peripheral neuritis, evidenced by paresthesias, numbness, and tingling; edema; dizziness; tremors; muscle cramps; psychotic reactions characterized by depression, disorientation, or anxiety; hypersensitivity (including rash, urticaria, pruritus, fever, chills, arthralgia, eosinophilia, and, rarely, hepatitis); constipation; difficulty in micturition; dyspnea; paralytic ileus; lymphadenopathy; splenomegaly; blood dyscrasias, consisting of reduction in hemoglobin and red cell count, leukopenia,

agranulocytosis, and purpura; hypotension; paradoxical pressor response.

DOSE

Initiate therapy in gradually increasing dosages, adjust according to individual response. Start with 10 mg 4 times daily for the first 2 to 4 days, increase to 25 mg 4 times daily for balance of first week. For second and subsequent weeks, increase dosage to 50 mg 4 times daily. For maintenance, adjust dosage to lowest effective level, particularly the incidence of toxic reactions, particularly the L.E. cell syndrome, is high in the group of patients receiving large doses of Apresoline. In a few resistant patients, up to 300 mg Apresoline daily may be required for a significant antihypertensive effect. In such cases, a lower dosage of Apresoline combined with a diuretic, reserpine, or

both may be considered. However, when combining therapy, individual titration is essential to insure the lowest possible therapeutic dose of each drug.

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Tablets: 10 mg (pale yellow, dry-coated); bottles of 30, 60, 100 and 1000.
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Consult complete literature before prescribing.

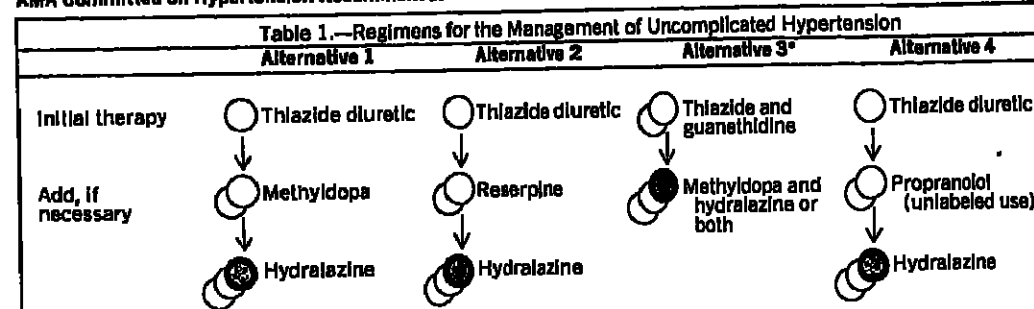
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...key component in the "guideline" antihypertensive regimens

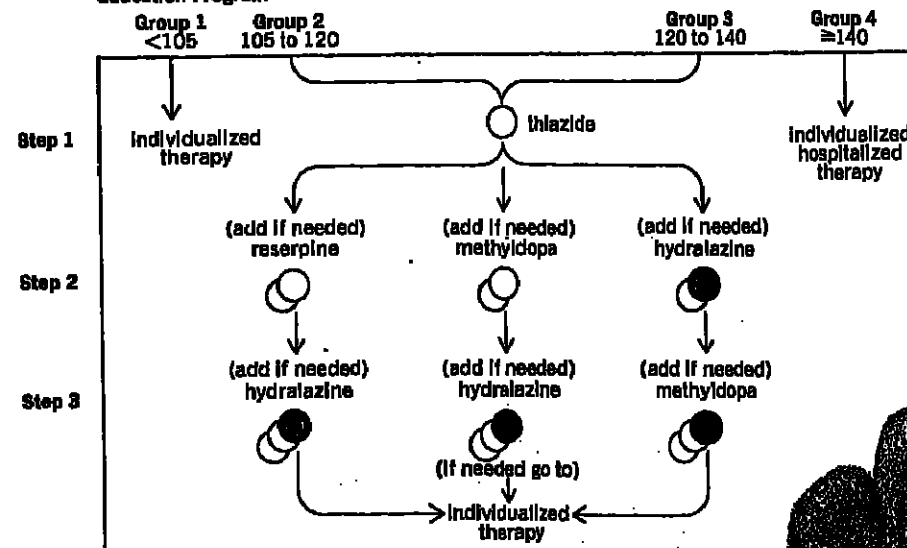
AMA Committee on Hypertension Recommendations



*In patients who cannot tolerate guanethidine, alternatives 1 or 4 may be given a therapeutic trial, but treatment should be initiated with both the diuretic and methyldopa or propranolol.

**Apresoline...
included in all four
treatment plans by the
AMA Committee⁶**

Recommendations by the Hypertension Task Force of the National High Blood Pressure Education Program

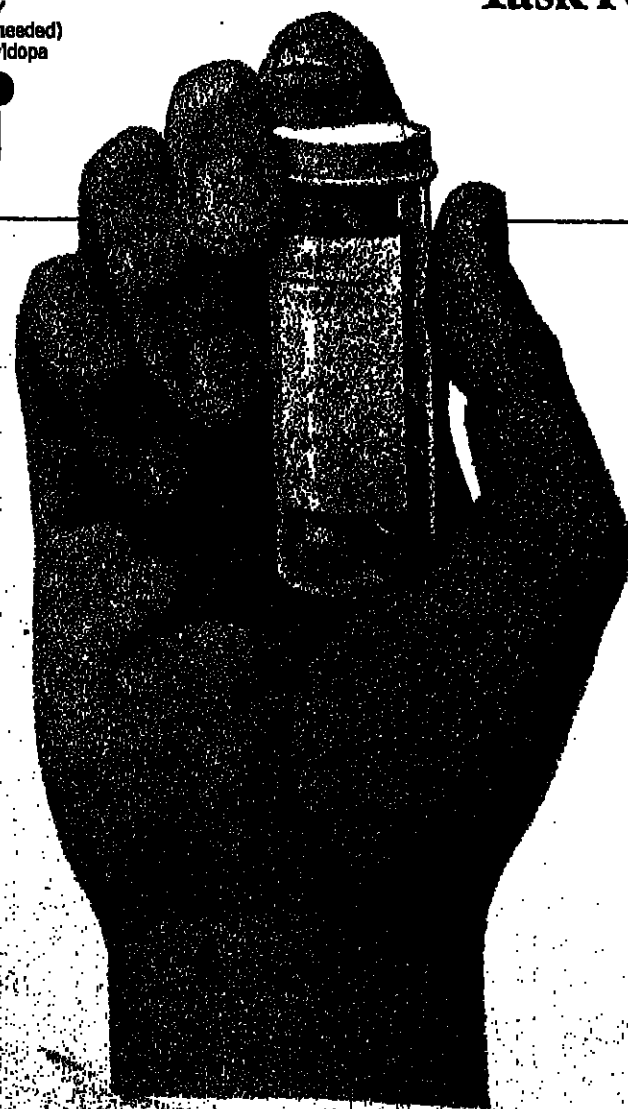


Therapeutic Objective: Diastolic pressure under 90 mm Hg, or, if untoward effects cannot be tolerated, under 100 mm Hg.

used effectively in the landmark VA studies^{8,9}

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**An antihypertensive
idea whose time
has come**



**Apresoline...
recommended second
and third step therapy
by the Hypertension
Task Force⁷**

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C I B A

Wednesday, April 14, 1976

EDITORIAL CAPSULES

...brief summaries of editorials or comments in current medical and scientific journals.

Lower Coronary Deaths?

...a recent decline in coronary mortality has been reported from two countries, the USA and Australia.

In 1968 there was an important change in the International Classification of Diseases affecting coronary heart disease and related causes of death, and there is a theoretical possibility that the recent decrease is an artifact.

...its lack of specificity weighs against its being due to improved treatment of myocardial infarction. Gordon and Thom believe that they have identified at least two relevant factors. Firstly, there has been a steady decline in mortality from hypertension, an important factor in most cardiovascular diseases—though mortality from hypertension was declining before the recent change in coronary mortality. The main reason, they suggest, is a decline since 1968 in mortality from influenza and pneumonia—diseases known to influence the death rate of coronary disease. Support for this view comes from the finding that the decrease in coronary deaths has been mainly in the months November to February, the peak months for mortality from respiratory disease. . . . (Editorial, *Brit. Med. J.* 1:58, Jan. 10, 1976)

Brain Damage In Sports

...Gronwall and Wrightson now seem to have taken the question of brain damage [in sports] a stage further. They used a simple test in which their patients were required to add serial numbers presented at different speeds by tape recorders. A group of healthy adults, who had been twice concussed, when so tested, were unable to 'process information' as rapidly as members of a similar group, matched for severity, who had sustained only a single head injury. Although recovery was slower in the twice concussed, in both groups the processing ability eventually returned to normal. Could a larger number of even mild concussive episodes permanently reduce the speed of information processing? Gronwall and Wrightson, having no data of their own on which to argue this point, turned to Roberts' clinical study on brain damage in boxing—a particularly thorough investigation of the possible effects of repeated blows to the head. Although Roberts had done no tests specifically designed to measure the rate of information processing, they felt that his findings, combined with their own observations, justified the conclusion that, in the 'general area of concussion-like syndromes,' repeated blows to the head can result in cumulative damage to the brain. They end their report: 'Whatever the mechanisms for this fall-off in intellectual performance, doctors do have a duty to convince the controlling bodies and participants in sports where concussion is frequent that the effects are cumulative and that the acceptance of concussion injury, though gallant, may be very dangerous.' (Editorial, *The Lancet* 1:401, Feb. 21, 1976)

IN CONSULTATION

What's New and Important About Goiter in Children?



The Consultant

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BEFORE THE INTRODUCTION of iodized salt in the 1920s, iodine deficiency goiter was prevalent among American children, especially in the "goiter belt" which included the Appalachian Mountains region, the Great Lakes area and the North West. Studies in these areas indicated that as many as 50% of school children had demonstrable goiter, with a distinctly higher prevalence in girls. Following the introduction of iodized salt, however, the prevalence of childhood goiter dropped significantly. Although the use of iodized salt was not universal, it is probable that this form of iodine supplementation was the most important factor in reducing goiter prevalence.

Recent studies indicate a low but persistent goiter prevalence in American children. There are some indications that the prevalence of goiter in children may be increasing. The etiology of this persistent goiter is not well defined, but it is unlikely that iodine deficiency is the underlying cause. On the contrary, nutritional surveys and the observation of falling average values for radioactive iodine uptake indicate a rising trend in iodine intake. Bread made with iodine dough conditioners, milk from herds receiving iodine along with other mineral supplements, and iodine containing food dyes have been implicated as largely unrecognized sources of increased iodine intake. It is probable that the average iodine intake of American children is currently two to four times the recommended daily allowance.

In assessing the clinical implications of these recent findings it is important to note that children with mild thyroid enlargement examined in recent large scale surveys have seldom shown abnormalities of thyroid function as indicated by clinical exam or by serum thyroxine or protein-bound iodine measurements. However, some have had moderately firm thyroid glands on clinical exam, possible of the Hashimoto type. Children with thyroid enlargement, particularly if the gland is firm or nodular, merit a thorough evaluation of thyroid function. In light of current information, it should not be assumed that the enlargement is the result of iodine deficiency.

What is the prevalence of childhood goiter in the U.S.?

Most recent studies have reported goiter in 5 to 10% of school age children, with a distinctly higher prevalence in girls. Consistent racial differences in the occurrence of goiter have not been demonstrated. Although previously there were marked regional patterns to the occurrence of goiter, these patterns are now less distinct.

What is the character of childhood goiter, i.e., diffuse or multinodular?

Most childhood goiter identified in field surveys consists of a mild, diffuse enlargement of the thyroid gland. In most cases the enlargement is detectable only by palpation and is not readily visible. Multinodular thyroid enlargement is relatively uncommon in children. Clinical studies indicate that when nodular goiter is encountered, the underlying pathology is frequently chronic lymphocytic thyroiditis.

What are the methods of assessing iodine status?

The most useful measure of iodine intake is urinary iodine excretion expressed in relation to urinary creatinine (μg iodine per gm creatinine). This measure will tend to reflect recent iodine intake. For this reason, testing urine samples on several different days will give a more accurate indication of the usual iodine intake.

What are the patterns of iodine intake in the U.S.? Are there children with deficient intake of iodine, and under what circumstances does this occur?

Some regional differences in iodine intake are suggested by regional differences in average radioactive iodine uptake results. However, more important than regional differences is the fact that iodine intakes in all regions of the U.S. appear to be well above requirements. There may be children with deficient iodine intakes in the U.S., but such an occurrence would be highly unlikely except in isolated areas where potential iodine sources such as commercially produced bread, milk, fish and iodized salt were less available.

What are the possible consequences of inadvertent high iodine intake?

Intake of high levels of iodine either inadvertently or for treatment of asthmatic conditions may cause goiter in some persons. This goiter is generally reversible when excess intake is curtailed. In persons who have been chronically low or deficient in iodine intake, a sudden increase in available iodine may lead to thyrotoxicosis. High levels of iodine intake during pregnancy may produce goiter in the fetus. There have also been reports of cretinism in infants associated with excessive maternal iodine ingestion during pregnancy.

Next In Consultation

DR. EARL BENEDICT BROWN, Assistant Professor of Medicine, Columbia University College of Physicians and Surgeons, and Attending Physician, Robert A. Cooke Institute of Allergy, Roosevelt Hospital, New York City, will discuss new developments in allergy and clinical immunology, forms of testing for atopy, the role of IgE in the pathogenesis of allergic manifestations, the reliability of skin tests, and the use of cromolyn sodium in asthma.

Injected Sponge Avoids Surgery in Malformed Cord

Medical Tribune Report

DALLAS—A new technique for intraparenchymal embolization of arteriovenous malformations of the spinal cord occludes the vascular malformation with an expandable embolus. Dr. J. L. Ausman, department of neurosurgery, University of Minnesota, explained at the Joint Meeting on Stroke and Cerebral Circulation here that small coils of Ivalon, a polyvinyl alcohol sponge are injected into the feeding vessels leading to the deformation. The emboli travel into the malformation where they expand and eliminate the problem.

Other embolization techniques, Dr. Ausman said, occlude the feeders to the malformation at a distant point, which allows the malformation to persist. His technique, on the other hand, allows intraparenchymal obliteration of the malformation.

Dr. Ausman cited one case study. A 24-year-old man with intramedullary high thoracic spinal A-V malformation presented with paresis of the left lower extremity. Two separate embolizations were necessary to occlude the malformation. The paresis condition improved and angiography confirmed obliteration of the malformation.

Some physicians prefer not to treat patients with symptomatic intramedullary arteriovenous malformations because of the risk of paralysis, the neurosurgeon pointed out. Treatment ranges from ligation or embolization of the feeding vessels to direct surgical removal of the malformation. The technique described by Dr. Ausman eliminates the need for surgery.

Don't Miss

THE GOOD DRUGS DO
Edited by the famous clinical pharmacologist, Dr. Lasagna, designed to be removed from Medical Tribune for your waiting room. It begins on Page 13.

FOR YOUR PATIENTS

ACTH Assay 'Premature' as Lung Ca Screen

Continued from page 1

answered are why ACTH should be produced in the lung at all and when this potential for ACTH secretion develops, Dr. Yalow emphasized in discussing her research at a symposium on pulmonary disease sponsored by the New York Academy of Medicine.

The situation is further complicated, she continued, by the possibility that heavy smoking or other insult to the lungs will prove a factor. Preliminary findings have yielded evidence that the lung tissues of heavy smokers may produce and secrete ACTH even if no cancer is present, she said.

Outlining the progression of current studies, Dr. Yalow said that plasma was obtained from patients with two forms of Cushing's syndrome—those with "pituitary" Cushing's syndrome and those with the so-called ectopic ACTH syndrome that is associated with secretion of ACTH by nonpituitary neoplasms.

Assays indicated that the major fraction of immunoreactive ACTH in patients having the ectopic ACTH syndrome was in the region of a larger molecular weight form now termed "big" ACTH, the biologically inactive form thought to be a precursor of the authentic "little" ACTH, Dr. Yalow said. Patients with pituitary Cushing's syndrome showed considerable variation—some samples had primarily little ACTH, others primarily big, and still others a mixture.

Plasma Levels Differed

Plasma levels of the hormone differed markedly, Dr. Yalow reported. Most patients in the pituitary group had plasma ACTH levels on the order of 100 to 500 picograms/ml while most of those in the ectopic group had values of 1,000 pg/ml. By contrast, circulating ACTH levels in normal persons who do not smoke are about 10 pg/ml (afternoon test).

The next step was to measure the biologic activity of big ACTH, Dr. Yalow explained, and to do so she and colleagues tested the primary tumor from patients with ectopic ACTH syndrome and then moved on to study other patients with elevated values of plasma ACTH but without clinically detectable Cushing's syndrome. The big ACTH turned out to have relatively low biologic activity.

One key observation has been that ACTH cannot be detected in normal adult lung but that immunoreactive ACTH is found in virtually all samples of tissue from primary carcinoma of the lung or from metastases of the pri-

mary tumor, Dr. Yalow said. It has not been found in tissues obtained from metastatic disease in the lung caused by other tumors.

Furthermore, concentrations of ACTH in lung cancer tissues from patients without clinical Cushing's syndrome are far lower than those in patients with the syndrome, the investigator noted—yet elevations of plasma ACTH (above a cut-off level of 150 pg/ml) were seen in 50 to 60% of patients having carcinoma of the lung in the absence of Cushing's syndrome, in about 30% of those with chronic obstructive pulmonary disease, and in only 6% of controls.

Such findings seemed to suggest that plasma levels could be used as a way

of detecting occult disease, but Dr. Yalow said the possibility must be discounted at present because studies have clearly shown that some patients with low values have proved to have carcinoma of the lung at surgery or autopsy while others with elevated values did not.

False Positives and Smoking

False negatives may occur in patients who have small, slow-growing tumors, according to Dr. Yalow. An explanation of the false positives, in her opinion, could be that heavy smoking or other lung insult might produce "massive histologic changes" in the lung without causing invasive carcinoma.

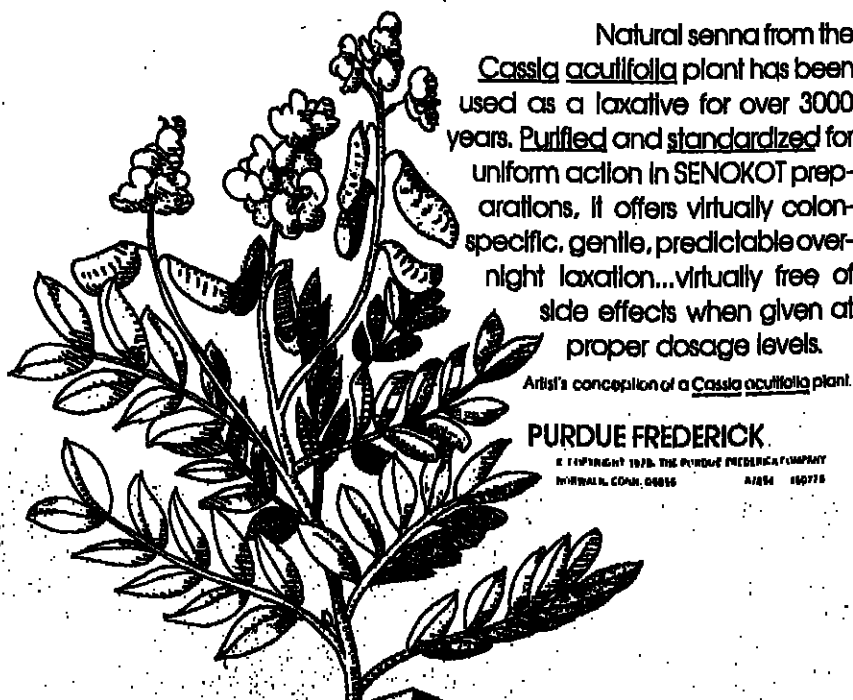
Dr. Yalow cited an experiment on smoking dogs which demonstrated that the lung tissues of one animal displayed marked histologic changes and contained ACTH even though this dog did not have invasive cancer. Lung tissue from animals not showing such changes did not contain the hormone.

Early reports on lung cancer patients do suggest that lower values of plasma ACTH are associated with longer survival times, Dr. Yalow said. She added, however, that cancer cell type must be taken into account in evaluating such findings.

Cooperative studies between her laboratory and pathologists in other VA hospitals are in progress, she noted, with the goal of finding out when "in the progressive changes in the lung from normalcy to invasive cancer"—ACTH production begins.

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Artist's conception of a *Cassia acutifolia* plant.

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Most TB Dormant for Yrs.

Medical Tribune Report

BALTIMORE—Three-fourths of the people with tuberculosis today show radiologic evidence that the disease has been dormant for many years, Dr. W. Head, of the Arkansas State Department of Health, told a medical symposium here.

In fact, he added, "Eleanor Roosevelt had tuberculosis as a teenager that went unrecognized until in her old age he was given steroids, and the infection reactivated and killed her."

Child Safety Through Anthropometry



As a result of a recent gathering of 41 specific measurements of children by the U. of Michigan Highway Safety Research Institute, manufacturers of children's products now have at hand a collection of child anthropometric data applicable to product safety design standards.

Men's Temperature Changes Equated to Menstrual Cycle

Medical Tribune World Service

AUCKLAND, NEW ZEALAND—Men undergo a "menstrual" temperature cycle similar to that of women except for an equivalent of the later part of the luteal phase, according to a study carried out in Australia.

Reporting this finding to the Royal Australasian College of Physicians here, Dr. Margaret Henderson, of the Search Biological Laboratories in Lower Templestowe, Victoria, Australia, said she studied 25 men in good health, ranging in age from 20 to 56. She had earlier noted that some men experienced asthma, migraine, depressed moods and indulged in alco-

holic bouts periodically for no clear reason.

Since many of these events occur in menstruating women, Dr. Henderson wondered whether there was some hormonally-related cycle in men.

The men recorded temperatures in the mouth and rectum night and morning for up to six months. They also wrote down their hours of sleep, changes in mood and emotions and any signs of stress. Twenty of the men were living with women and the women recorded their own temperature changes in the mouth and vagina.

In ten of the men, 34 recognizable cycles were revealed. Another five showed some form of regular illness or need for medication. Seven showed no effects at all and three did not provide sufficient data. Hormonal changes and their mechanisms still need to be studied, said Dr. Henderson.

Some of the males had shown individual symptoms, such as very severe pain in the rectum for short periods.

"I tracked this in two men and it seemed to correspond with a menstruation period," she said.

Speaking of her findings in general, Dr. Henderson said it was found that following a mid-cycle drop, male temperatures rose to a high level for two to five days, in line with what happens in women. But later the male temperature dropped and this was the only significant difference from women.

Close Synchronization

Dr. Henderson said other studies had previously shown that where two women live together they achieve close synchronization in their menstrual periods in some unexplained way. She found this was also true where a man and woman lived together.

In the cases studied, the male temperature showed a mid-cycle drop at about the same time or even on the same morning as the woman living with the man experienced this. Some of the men were also having sex relations with girl friends, but the synchronization still followed the wife with whom the man was spending more time.

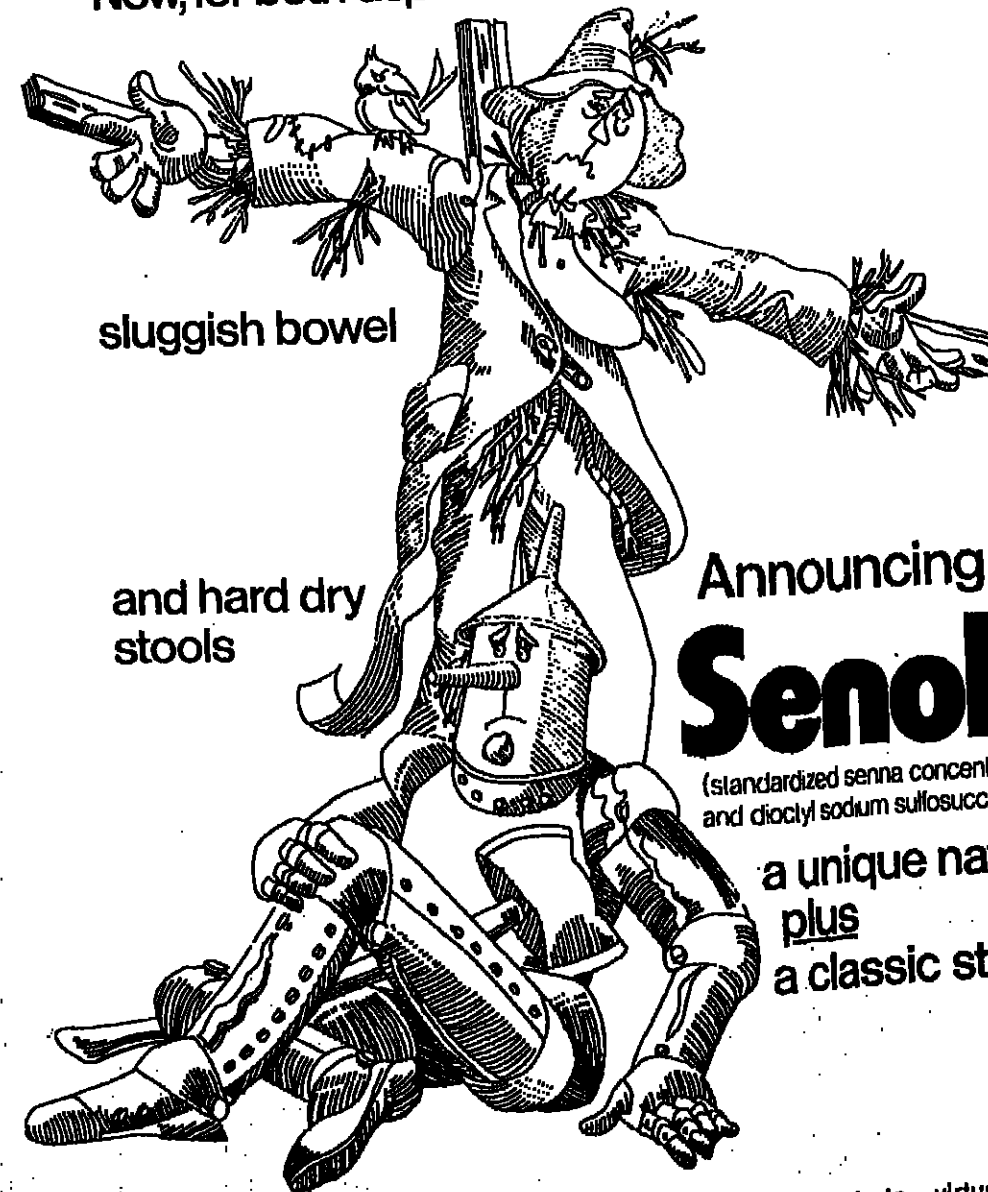
Individual characteristics of morning temperature patterns in three males showed "postovulatory" peaks. Two homosexual males living together (but not sex partners with each other) showed the characteristic mid-cycle synchrony. Some rhythm was evident in males not living with women, but an exact cycle definition was not possible, Dr. Henderson said.

The cycle in men seemed to vary from 17 to 35 days.

It was also established that when a woman living with one of the men began taking oral contraceptives the male cycle would fail to synchronize with her induced periodicity. The characteristics of the male cycle were significantly altered, usually to an 18 or 19 day cycle unconnected with hers.

Dr. Henderson hopes that practical benefits from this study will include a better understanding of fertility and new methods of dealing with menstrually-associated conditions in both men and women.

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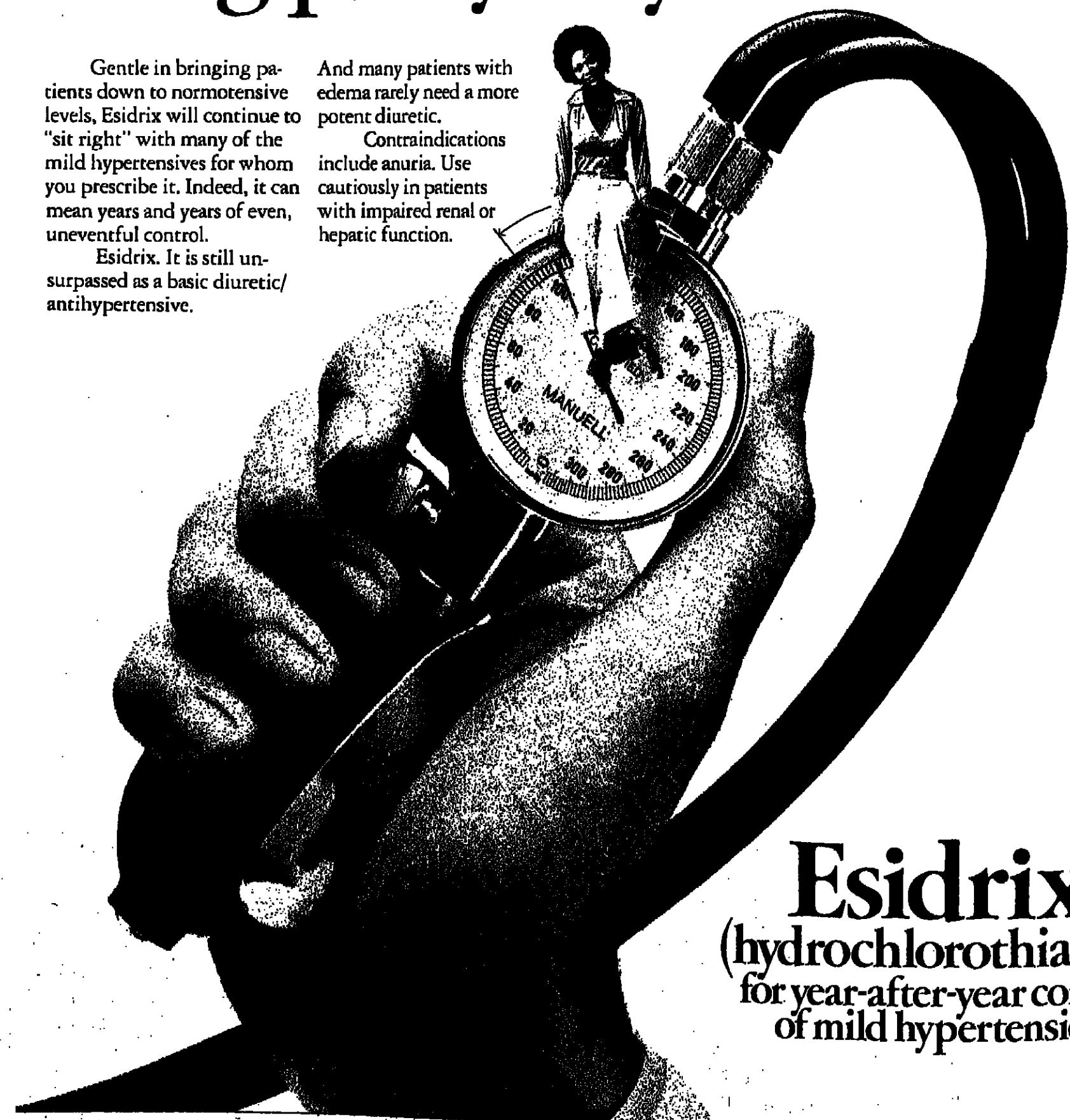
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WARNINGS

Use with caution in severe renal disease. In patients with renal disease, thiazides may precipitate azotemia. Cumulative effects of the drug may develop in patients with impaired renal function.

Thiazides should be used with caution in patients with impaired hepatic function or progressive liver disease, since minor alterations of fluid and electrolyte balance may precipitate hepatic coma.

Thiazides may be additive or potentiative of the action of other antihypertensive drugs. Potentiation occurs with ganglionic or peripheral adrenergic blocking drugs.

Sensitivity reactions are more likely to occur in patients with a history of allergy or bronchial asthma. The possibility of exacerbation or activation of systemic lupus erythematosus has been reported.

Usage in Pregnancy: Usage of thiazides in women of childbearing age requires that the potential benefits of the drug be weighed against its possible hazards to the fetus. These hazards include fetal or neonatal jaundice, thrombocytopenia, and possibly other adverse reactions which have occurred in the adult.

Nursing Mothers

Thiazides cross the placental barrier and appear in cord blood and breast milk.

PRECAUTIONS

Periodic determination of serum electrolytes to detect possible electrolyte imbalance should be performed at appropriate intervals. Observe patients for clinical signs of fluid or electrolyte imbalance (hypotension, hypochloremia, hypokalemia, hyponatremia, hypochloremic alkalosis, and hypotension).

Serum and urine electrolyte determinations are particularly important when the patient is vomiting excessively or receiving parenteral fluids. Medication such as digitalis may also influence serum electrolytes. Warning signs are dryness of mouth, thirst, weakness, lethargy, muscular fatigue, hypotension, oliguria, tachycardia, and gastrointestinal disturbance such as nausea or vomiting.

Hypokalemia may develop with thiazides as with any other potent diuretic, especially during brisk diuresis, when severe diarrhea is present, or during concomitant administration of diuretics or ACTH.

Interference with adequate oral intake of electrolytes will also contribute to hypokalemia. Clinical signs may include metabolic effects of hypokalemia, especially with reference to myocardial activity.

Any chloride deficit is generally mild and usually does not require specific treatment except under extraordinary circumstances (as in liver disease or renal disease). Dilutional hyponatremia may occur in edematous patients in hot weather; appropriate therapy is water restriction rather than administration of salt, except in rare instances when the hyponatremia is life-threatening.

In actual salt depletion, appropriate replacement is the therapy of choice.

Transient elevations in plasma calcium may occur in patients receiving thiazides, particularly in those with hyperparathyroidism. Pathological changes in the parathyroid glands have been reported in a few patients on prolonged thiazide administration.

Hyperuricemia may occur or frank gout may be precipitated in certain patients. Insulin requirements in diabetic patients may be increased, decreased, or unchanged. Latent diabetes may become manifest during thiazide administration.

Thiazide drugs may increase the responsiveness to tubocurarine. The antihypertensive effect of the drug may be enhanced in the post-sympathetomy syndrome to norepinephrine. This is not sufficient to therapeutically use.

If nitrogen retention indicates onset of progressive renal impairment, consider withholding or discontinuing diuretic therapy.

Thiazides may decrease serum PBI levels without signs of thyroid disturbance.

ADVERSE REACTIONS: Gastrointestinal—nausea, vomiting, cramping, diarrhea, constipation, jaundice (intrahepatic cholestasis), pancreatitis, Central Nervous System—dizziness, vertigo, paresthesias, headache, xanthopsia, Dermatologic—hypersensitivity—purpura, photosensitivity, rash, urticaria, necrotic angitis, Stevens-Johnson syndrome, and other hypersensitivity reactions.

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Wednesday, April 14, 1976

MEDICAL TRIBUNE

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The Only Independent Weekly Medical Newspaper in the U.S.

Medical Tribune

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Enough of Pessimism: Part III

OUR POVERTY goes beyond a lack of leadership. It extends to a malaise of the spirit of our people. Indeed such is the pathology that, even if the Messiah should appear, he or she would either go unrecognized or, if recognized, would soon be chopped down to size. At the same time this country has turned its back on optimism and is becoming a nation of pessimists.

In this country optimism was at its peak early during times of great poverty, hardship, and amid unmerciful ravages of disease. But Franklin's optimism was justified by events. Great increases in knowledge and enormous improvements in agriculture, medicine, and technology liberated many humans from much of the drudgery and pain that had previously been their lot. But the behavior of humans is weird and

wonderful. Far from feeling gratitude toward benefactors or admiring the great edifice of knowledge that makes their comforts possible, they have now turned sour and their attitudes are reflected by their chosen representatives.

During most of the country's history, perhaps its greatest assets were its faith in progress, its can-do spirit. Sometimes exuberance was overdone but better than the opposite, as any experienced scientist can testify. The research worker who is convinced ahead of time that experiments will be fruitless seldom is proved wrong in that judgment. It is the optimists who achieve.

PHILIP H. ABELSON
Editorial
Science, Jan. 9, 1976

Medical Ethics—The Teaching Of

JUST ABOUT 40 YEARS AGO, the subject of medical ethics was covered in a one-hour lecture to the senior class at one of our leading medical schools. The lecturer was an invited one—the president of the local medical society. The lecture itself consisted of a diatribe directed at three targets: abortionists, fee-splitters, and proponents of state medicine. Times have changed since then and in many ways. Perhaps symptomatic of the change is that abortion is legal today although still controversial; that state medicine would certainly not be subject to a current diatribe on the basis of ethics; and that fee-splitters, although still subject to criticism, hardly merit discussion since their numbers must be vanishingly small in the medical economy of our present era.

The foregoing is not meant to imply that medical ethics had short shrift in the past. All medical students early in their studies were made aware of the dictum, *primum non nocere*. Osler's book *Aequanimitas*, which medical students in the earlier decades of this century were usually exposed to, was imbued with the consciousness of ethical behavior and emphasized "the practice towards patients of the Golden Rule of Humanity as announced by Confucius: 'What you do not like when done to yourself, do not do to others.'"

It is of interest that Osler suggested a bedside library for medical students, which, he said, if read for half an hour before going to sleep would help "to get the education, if not of a scholar, at least of a gentleman." It is likely that by gentleman he meant one whose behavior is of the highest standards. The books he listed were: the Old and New Testaments, Shakespeare, Montaigne, Plutarch's Lives, Marcus Aurelius, Epictetus, Religio Medici, Don Quixote, Emerson, Breakfast-Table Series of Oliver Wendell Holmes. How many medical students of today have been exposed to these books in any depth?

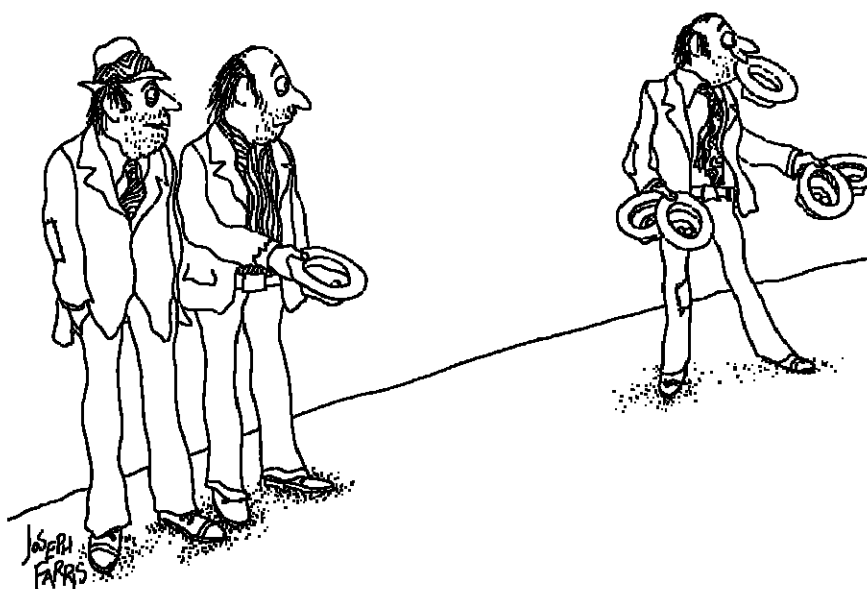
But he that as it may, there has been a noteworthy expansion in the organized teaching of medical ethics in our medical schools. An article in the March 8 issue of *JAMA* by Robert M. Veatch, Ph.D. and Shurman Solitto of the Institute of Society, Ethics and the Life Sciences, reports on surveys of medical ethics teaching in medical schools in 1972 and 1974. Of 95 schools in 1972, 14 stated that medical ethics were not taught; in 1974, 10 of 107 schools made such a statement. Four in 1972 and six in 1974 had required courses, while 37 in 1972 and 47 in 1974 had elective courses. Incorporation into other courses and special programs had much wider representation in 1974 than in 1972.

The article points out some of the areas of difficulty, of problems and of progress. Certainly the specifics of informed consent are on an entirely different level of consideration today as compared with the past. The areas of potential harm today, as of potential good, are of a different order of magnitude than they were in the past and the problems of what may be done and may not be done, of what should be done and should not be done, require explicit and detailed consideration.

Reducing MI Mortality

CLINICAL QUOTE: "Of the 108 patients in the treated [with external-pressure cardiac assist] group, seven patients, or 7%, died, compared with 17 patients, or 15%, in the control group. Cardiac failure, class 3 or 4, was

observed in 6% of the treated group, 15% of the controls. A total of 89% of the treated patients had changed in clinical status at discharge to Class I, compared to 77% of the controls." (Dr. Ezra A. Amsterdam. See p. 1.)



"He can't help it. He's Type A behavior."

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LETTERS TO TRIBUNE

Jogging to an End?

Jogging must be joking—at least in my opinion. The need for muscular movement stems from requirements demanded by the brain which can survive only with O₂, water and calories. They are fulfilled by eating, drinking, and breathing. These are gathered in by the use of the musculoskeletal structures, the lungs and the gastrointestinal tract—all under cerebral guidance. Reproduction of the human brain is the sole purpose of the energizing forces which preserve, assist in growth and produce movement.

Therefore, the use of the musculature, with cardiopulmonary support, is primarily the function of survival. Also, of some concern is the ability of the human creature to survive the hazard of the environment—by whatever methods necessary—again requiring muscular energy.

The individual who has not made use of these functions may suffer the pains and pathos of cardiopulmonary disease or hypertensive frustration.

Why, then, are we recommending the aimless and useless exercise of jogging—or weight lifting? Shouldn't walking, running or jogging be a means to an end like picking up the groceries, delivering the mail, or chasing the villains?

Isn't jogging nothing but running in circles?

It is suggested that exercises, so advised by physicians, be related to productive ends, like survival's intent. If the individual can find nothing for himself, let him become involved in the community.

He can exercise by cleaning up the parks and beaches. He can carry away the trash of our streets. He can bring food to the elderly and disabled. He can walk infants and children and entertain the sick. He should use his jogging for productive and creative ends for which cerebral-muscular movement was intended. Then he can truly avoid the hazards of hypertension, atherosclerosis and cardiac disease.

If you recommend jogging, why not

make it a means to an end—production? Then you will fulfill the requirements of life itself.

Jogging shouldn't be joking. Let's form a constructive exercise corps and help our environment as well as ourselves.

A. M. GROSSMAN, M.D.
Beverly Hills, Calif.

Oops!

I was pleased by your thorough and accurate reporting of the data which I presented at the annual Assembly of the American Academy of Physical Medicine and Rehabilitation.

There is one significant error in paragraphs 7 and 8 to which I would like to draw your attention. Please review the enclosed information and, if at all possible, make the necessary correction.

JULIE G. BOTVIN, M.D.
Pomona, Calif.

Dear Dr. Botvin: If only we had your picture, we would never have made such a silly error in paragraphs 7 and 8 as to refer to you as he. Our apologies—Editor.

PATIENT EDUCATION can begin in your waiting room if you'll remove the special section from this paper titled **THE GOOD DRUGS DO** and put it in your waiting room. Edited by the top pharmacologist, Dr. Louis Lasagna, it will help build doctor-patient relationships. It begins on Page 13

CIBA

Guidelines Offered on Prophylactic Nitroglycerin in Angina Pectoris

By HARRIET PAGE
Special Tribune Correspondent

PALM SPRINGS, CALIF.—Medical treatment of angina pectoris is often ineffective because it's not optimal medical treatment. And one of the mainstays of optimal treatment is prophylactic use of nitroglycerin.

That was the thrust of two separate arguments presented here at the annual meeting of the American College of Angiology.

Patients Predict Episodes

Dr. Ezra A. Amsterdam, Associate Professor of Medicine and Chief of the Coronary Care Unit at the University of California, Davis, said he and his associates had just finished a questionnaire of 115 angina pectoris patients referred for angiography. "Only 25% of these patients had ever been told about the use of prophylactic nitroglycerin, and many of them who have been told, don't use it. So there's a two-way problem here—education by the physician and response by the patient."

"Far fewer angina patients would be considered refractory if appropriate medical therapy were used," Dr. Amsterdam said.

"Many angina patients can predict with some degree of accuracy when they will have an anginal episode—emotional stress, sexual intercourse, climbing stairs, walking across the parking lot. Taking nitroglycerin before any one of these activities will reduce the angina or alleviate it entirely," Dr. Amsterdam said.

Dr. Peter M. Yurchak, Associate Professor of Medicine at Harvard Medical School, also noted that medical treatment of angina is "effective if it's optimal, but most patients don't receive optimal treatment."

"Unless internists and cardiologists are willing to spend the time to administer optimal treatment, then they pass the baton to their surgical friends," Dr. Yurchak said.

Whether medical treatment of angina will help to prevent myocardial infarction or arrhythmias is still not proved, Dr. Yurchak continued, "but much can be done to ameliorate angina."

"Details of medical management are often ignored, though, because the physician is dazzled by the accessibility of the surgical attack on the problem."

Practical Points

There are a number of simple, practical points in nitroglycerin therapy that are often overlooked, Dr. Yurchak noted. First, he said, medication must be properly stored so it won't lose its potency. It should be shielded from ambient light by keeping it in a dark bottle. It should be tightly stoppered to avoid loss of the agent by evaporation. Tablets should be kept in a small container so tablets won't rub against each other and be degraded.

It's also important, Dr. Yurchak continued, that no other agent be incorporated with nitroglycerin because other agents will absorb it and result in a reduction of potency. Tablets should be stored at room temperature, not carried in a watch pocket at body temperature,

which will hasten degradation. Also, tablets will lose effectiveness with time and should be replaced every six months.

Many patients aren't told the importance of maintaining the tablet sublingually, rather than swallowing it, Dr. Yurchak added. Usually, patients report a tingling sensation on the tongue that is related to pharmacologic activity. Also, he said, patients should be advised to sit down when taking nitroglycerin to avoid the adverse effects of a possible sharp drop in blood pressure.

Finally, Dr. Yurchak said, "Patients should be urged to use tablets prophylactically—at the first sign of pain—and to continue at intervals until three tablets are used. If pain continues, then the physician should be called."

Reinforcing Instructions

There are a variety of booklets put out by drug companies and by the American Heart Association that are very useful in reinforcing the physician's verbal instructions to his patient, he added. Reinforcement is necessary, Dr. Yurchak said, "so the patient won't deny he's ever been told."

Beta adrenergic blockers are the "other pillar" for angina therapy, he noted, and patients can't be considered refractory to drug treatment "unless both agents have been used to full tolerance."

Dr. Amsterdam noted also that it is important for the physician to understand the hemodynamics of drugs and bypass surgery, both in prescribing therapy and in evaluating it. Clear, uncomplicated angina pectoris, he said, is a manifestation of coronary artery disease that, in turn, causes an imbalance between myocardial oxygen demand and supply.

Rational Evaluation

"If the demand exceeds the supply, then the result is angina. It's our thesis that only surgery can bring about a significant increase in supply, and that medical therapy reduces the demand. That's somewhat simplified, and there are overlaps," he noted.

The major factors that determine oxygen demand are contractility, blood pressure, and ventricular volume, which make up intramycardial tension and heart rate, Dr. Amsterdam said. And the effect of nitroglycerin is to reduce heart size, reducing myocardial tension by reducing volume. It does this, he said, by increasing venous dilatation, increasing vein capacitance, and dropping blood pressure.

Similarly, Dr. Amsterdam said, exercise training can also increase exercise capacity by acting as a medical intervention and reducing the circulatory load for a given effort.

Bypass surgery, on the other hand, results in a marked increase in exercise capacity but does this by increasing oxygen supply, the only therapy that can cause this response.

"Both approaches are rational," Dr. Amsterdam concluded, "but it's important to understand what you're doing and to evaluate patient response in a rational way."

The special section facing this page

THE GOOD DRUGS DO

Is a new therapeutic supplement of Medical Tribune prepared for patients and designed for placement in your waiting room as a public health service.

These supplements are dedicated to the physician-patient relationship. They seek to assure greater therapeutic compliance on the part of an informed patient in the interest of better medical care.

We trust that you will find these Medical Tribune supplements an aid in advising patients and helping them to understand your recommendations and therapeutic regimen.

To enable this effort to best fulfill its goals, we would appreciate any suggestion for improving them. Each issue of THE GOOD DRUGS DO prepared thus far has been devoted to a single indication. These presently comprise Depression, Hypertension, Nutrition and Vitamins, Alcoholism, Diabetes, Psychoses, Arthritis and Infections. An outstanding authority in each of these respective fields has prepared the issue under the general editorship of Louis Lasagna, M.D., Professor of Pharmacology, University of Rochester School of Medicine and Dentistry.

You can help advance the physician-patient relationship: Remove THE GOOD DRUGS DO supplement immediately following this page and place it in your waiting room.

Additional copies are available upon request.* We look forward to hearing from you.

Arthur M. Lasagna

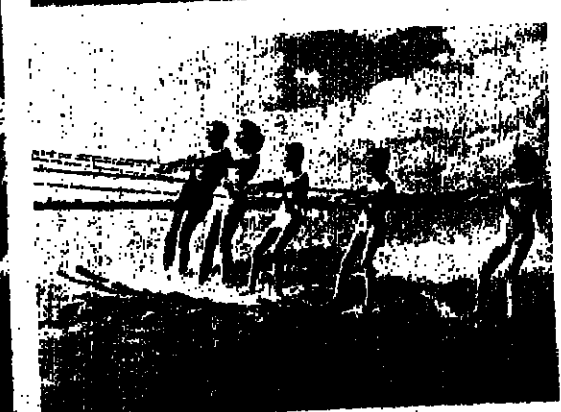
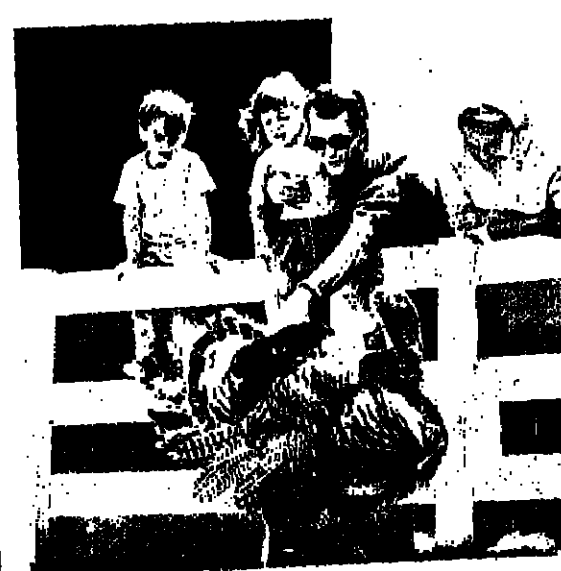
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THE GOOD DRUGS DO

to better your health

Treatment of alcoholism is salvaging lives



Medical Tribune THE GOOD DRUGS DO to better your health

is specially prepared for the waiting rooms of America's physicians to provide patients with accurate information about drugs, vitamins and foods their physician may prescribe.

Dr. LOUIS LASAGNA, Professor and chairman, Department of Pharmacology and Toxicology, University of Rochester School of Medicine and Dentistry, is editor of this service.

Each installment features a leading authority on a health problem of concern to the public and to physicians.

Introducing



Dr. Chafetz

Dr. MORRIS E. CHAFETZ, one of the world's foremost authorities on alcoholism, organized and served for five years as Director of the National Institute on Alcohol Abuse and Alcoholism, Department of Health, Education and Welfare.

Today he is Principal Research Scientist, Metropolitan Center for Planning and Research, at the Johns Hopkins University, a fellow of the Royal College of Health, the recipient of the Mt. Airy Gold Medal Award for distinguished service to psychiatry.

An associate clinical professor of psychiatry at Harvard Medical School and Director of Clinical Psychiatric Services at the Massachusetts General Hospital in Boston, Dr. Chafetz has written and collaborated on over 150 scientific articles and seven books, including *Alcoholism and Society*, *Liquor, the Servant of Man*, and *Frontiers of Alcoholism*.

He has served on numerous national and international bodies dealing with health, psychiatry and alcoholism.



How alcohol affects your health

by Dr. Morris E. Chafetz

Is alcohol a drug?

Yes, it is, a powerful one. Its chemical name is ethanol. It is the most commonly used drug in the history of man and in the world today. Its widespread—and ancient religious and social—use has blurred the realization that this mind-altering substance is in reality a drug. During Prohibition doctors wrote prescriptions for it for patients who needed it; one of its most common medical uses at that time was to deaden pain in cancer patients.

This blurring of the realities about alcohol has long prevented our coping with problems that its misuse creates. We all know people whose alcoholism has destroyed their lives and brought despair to their families—judges, Congressmen, Senators, artists, athletes, physicians, inventors, businessmen, electricians, plumbers, laborers. No group has been immune.

But we've only recently begun to see beyond hand-wringing and moralizing—that excessive use of alcohol is a problem that combines the chemistry

of the body and mind with psychologic stress, and that not everyone can drink; that if we think a "drunk" act by a TV comedian is funny and applaud him, we are really confused. Would we applaud someone stumbling, nodding and mumbling because he's loaded with heroin or cocaine? When we accept Carol Burnett, the great TV comedienne, opening a recent show demonstrating the harm of the excessive use of alcohol, by stating that her own life as a child had been made miserable because her parents were alcoholic, we've come a long way in understanding this drug and how to get control over it.

Can alcohol do good?

For most people, alcohol offers some mildly beneficial effects when used moderately in social and recreational ways. At the same time it has also been scientifically demonstrated that some people shouldn't touch alcohol at all. It must be remembered that alcohol was initially included in highly regulated

religious ceremonies and social customs as a means of enhancing the pleasurable feelings and meanings inherent in such rituals and customs. Even today, on a worldwide basis, it is in such religious ceremonies and in custom-regulated family settings that most individuals first use alcohol.

That alcohol has some beneficial effects is recognized by most people, but this does not mean that it cannot be misused—and unfortunately it often is.

Is alcohol dangerous?

Yes, alcohol—this drug which is so easily available—is a more dangerous substance than virtually every known medicinal drug. Its misuse—that is, excessive use—is dangerous. For millions of Americans it is so dangerous that they should never touch it. Its continued misuse results in an illness: alcoholism. One of the great problems in our use of alcohol is not recognizing that it is dangerous, that not everyone can tolerate alcohol without damaging himself in some way.

What is excessive use of alcohol?

Each individual has his own limitation. For one person, it might be one sip of wine, for another, even that might be too much; for still another, a glass of beer or an ounce of whiskey might be the limit. The failure to understand that each person has his individual limit before alcohol makes him intoxicated, incapable of good judgment and appropriate behavior and reactions, has helped to create the problem of alcoholism. Social pressure to "have another" is often the cause of the misuse of alcohol.

Each individual should know and accept his responsibility to himself and others not to use alcohol to excess—whatever his limit. And no one should pressure anyone to "have another."

Is alcohol related to disease?

The most recent report of the Secretary of Health, Education, and Welfare relates prolonged, heavy use of alcohol to certain diseases. These are cancer of the throat, mouth, and liver, one form of heart disease—cardiomyopathy—and cirrhosis of the liver. In addition, heavy drinkers die at younger ages than moderate drinkers. Among the groups with alcohol-related increased death rates, women have higher rates than men and the youngest age groups have the highest death rates of all.

Cultural attitudes influence drinking patterns.



Many people no longer see Red Skelton's drunk act as funny. Carol Burnett opened a TV show against alcoholism by pointing out how miserable her childhood was because of her parents' drinking.



Alcohol was first used, and still is, in religious ceremonies to enhance rituals, but became the most abused drug in the world.

Alcohol is particularly dangerous when other drugs, including those prescribed by your doctor or bought over the counter in a drugstore, are being taken. Its chemistry may complicate the chemistry of other drugs—and serious illness and even death can immediately follow. Drugs and alcohol do not mix. If you are taking medicine prescribed by your doctor, avoid alcohol.

How long has the danger of alcohol been recognized?

The misuse of alcohol—causing intoxication, which means in everyday terms an inability to function effectively and in a socially acceptable, responsible way—goes back to earliest times. The Bible's book of *Genesis* records the story of Noah being drunk.

What has taken place over the centuries is a drift away from religious and appropriate social use into devastating social misuse. This misuse was probably related to man's efforts to deaden the misery he felt in an increasingly complex and difficult physical, social and economic environment.

Is alcohol used medically?

Alcohol has a long history of medicinal use before modern research gave us better drugs for the control of pain, to relax people, to aid sleep. Before modern anesthetics were developed alcohol was used as an anesthetic—as you may recall from Melville's novel, *Moby Dick*. It was also used medically—and still is—as an appetite stimulant.



Alcohol was once used as anesthetic.

Depression, anxiety and alcohol

Depression is one of the most common findings in people with alcohol problems. Many people, when depressed, take alcohol as a form of self-medication. To "cheer up" they drink this mind-altering drug. Their depression may come from some disappointment, lost opportunity or rejection. In books and television such drinking is portrayed when the hero loses the girl or the job, gets "down in the dumps," and drowns himself in overdoses of alcohol to deaden the inner pain he feels. Because these "low" feelings arise from some situation, physicians often call these "reactive" or "situational" depressions.

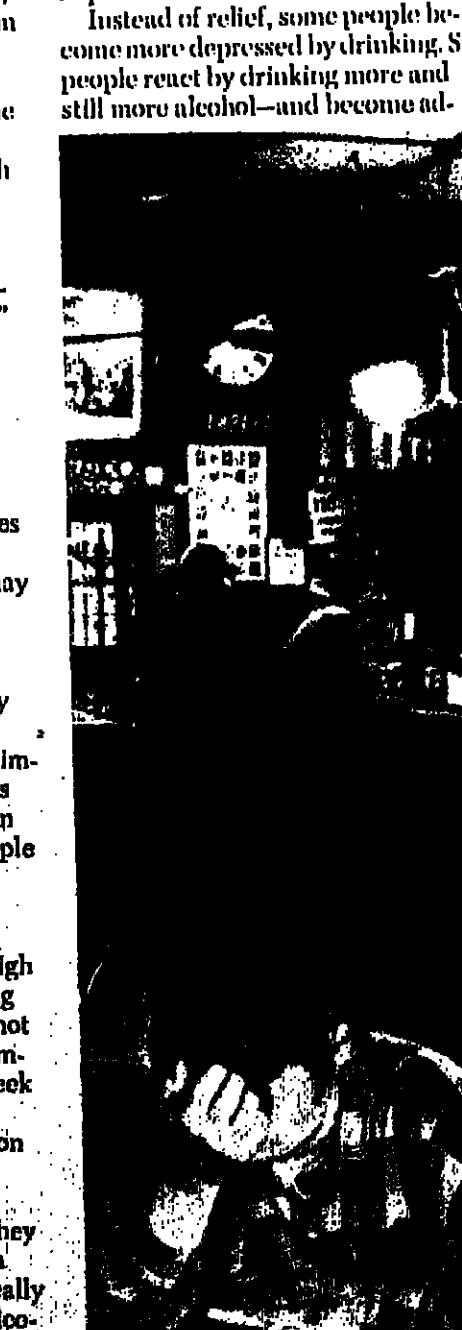
In other cases, people may "self-medicate" themselves with alcohol irregularly—turning to it when anniversaries of losses or painful memories occur. Or when holidays accentuate their loneliness. Anything that may make a vulnerable person feel defeated may lead to an episodic alcoholic bout. These incidents are not easily detected or dealt with in many cases because the depressed person tends to cover up—even to deny to himself—what hurts, including the losses of relationships. Feelings of rejection or humiliation can trigger some people into heavy drinking bouts.

Falling short of goals

In still other cases, people with high ideals constantly feel they are falling short of their goals—and they then not only feel badly disappointed in themselves but inadequate. They then seek relief in alcohol.

And in some people the depression may be of such a deep, intense and continuous nature, with feelings of overwhelming hopelessness, that they drink persistently. Such people can actually destroy themselves physically with the increasing quantities of alcohol they take to deaden their intolerable feelings of worthlessness and hopelessness.

Instead of relief, some people become more depressed by drinking. Such people react by drinking more and still more alcohol—and become addicted to alcohol.



Others who may get some relief from depression with alcohol then become fearful of giving up their self-administered "medicine" because they want to stave off their "blues." Often sick physically from their "drinking," they may see their sickness as a punishment for having "overdone it"—which helps them feel eligible for another round of drinking.

Change—an alleviating factor

Obviously, many factors contribute to depressed feelings and these factors are not the same in everyone. The depression can be alleviated by a change in the person's life—new friends, a new job, finding satisfaction and praise for his or her efforts at work, in a social situation like a club or church affair. Such changes reduce the "low" feelings that push many people into drinking. Anything that helps a person feel worthwhile will help to decrease his feeling "blue."

However, such changes in a person's life are not easily achieved—often partly as a result of a continued pattern of drinking—and such people may get significant help in achieving a new way of living and working from antidepressant medications under a doctor's supervision. There are two main groups of antidepressant drugs: the monoamine oxidase inhibitors and the tricyclics. These medicines, well known to physicians, lessen the heavy burden of depression and hopelessness that the individual feels, permitting other much needed treatment. For example, a depressed person who has turned to alcohol to the point where he has lost job opportunities or damaged relations with his family and loved ones, may feel very guilty and be unable to get a new grip on his own perspective on himself and what

Continued on page 20

Your questions on alcoholism answered

For whom is alcohol totally forbidden?

A person who has had severe alcoholism should never take alcohol. Most people who recover learn new ways of handling the stress and pain which they previously coped with by using heavy doses of alcohol. But alcohol puts to sleep those parts of the brain which contain recently learned information. That is why Alcoholics Anonymous says that for an alcoholic one drink is too much.

It is true a small number of severe alcoholics have gone back to taking alcohol without excessive use and without apparent trouble. There is good reason why doctors always ask: "Is it worth the risk of recreating the horrible misery you suffered with alcohol just to find out whether or not you are a part of a very small group?"

Severe alcoholics should never drink, nor should people who were ethically raised by attitudes of militant teetotalers. As for militant teetotalers, these good people should never take any alcohol because clinical observation shows, for reasons we do not fully understand, that if they do drink, they quickly become alcoholics.

Who should use alcohol with caution?

Children of alcoholic parents are at greater risk than the general population to develop alcoholism because studies show that 70% of the patients in alcohol clinics had people around them while they were young who had problems with alcohol. Since alcoholism is considered by many to be learned behavior, children of alcoholic parents should be careful. They should be cautious and controlled in how they take alcohol.

Also, people who have had liver disease, pancreas problems and ulcers of the stomach or intestines should use alcohol with caution. If you are undernourished or suffering an infection, you should restrict your use of alcohol. People who are on sleeping medications, antihistamines, tranquilizers or antismotion medication should use extreme caution in taking alcohol because when alcohol is combined with other drugs, its actions become unpredictable and dangerous. A number of deaths have been reported when alcohol was taken in combination with even small doses of safe drugs. People who will be driving their automobile should be cautious about their use of alcohol. Studies show that most moderate drinkers will have the same number of accidents as a person who does not drink; but with more than a very moderate amount of alcohol, the risk of automobile accidents is very high.

Who may use alcohol in moderation?

Anyone who does not suffer severe alcoholism, who does not have to observe the cautions listed above and one who has no moral or ethical stand

Continued on page 18

Advances in control of alcoholism



Historically, efforts to control abuse of alcohol go back to Biblical times. Hogarth, in his famous "Gin Lane" etching, portrayed its destructiveness in London in 1700s, about the same time that Dr. Benjamin Rush (with quill pen), America's first psychiatrist, began to urge its medical treatment here. Currier and Ives' print, "The Drunkard's Progress," aided the growing temperance movement which sought to outlaw drinking. Currier Nation (above) attacked saloons



with an axe to dramatize the temperance movement. The temperance leaders recognized health hazards of alcoholism but unfortunately alienated many who would have been their allies by insisting on absolute prohibition—not moderation. When Prohibition was enacted, it failed because most people are not abusers of alcohol and resented it. Today's efforts to curb abuse of alcohol, combining cultural, scientific and medical approaches, are beginning to make progress.

Attempts to treat alcoholism as a crime have been replaced by attempts to educate public and particularly police about alcoholism, its causes and its treatment. Cartoons below are from the World Health Organization's film on alcoholism which emphasizes that it is medically treatable. Abuse of alcohol is a worldwide problem.



The late Dr. E. M. Jellinek of Yale University (left), who formulated the concept of alcoholism as a disease, and "Bill W." (right) who co-founded Alcoholics Anonymous with "Dr. Bob," made enormous contributions to different aspects of the treatment of alcoholism.



Recovered alcoholics like Marty Mann (left, advising Susan Hayward on *I'll Cry Tomorrow*, movie about Lillian Roth's recovery) have played a major role in



the struggle against the disease. Mann, who founded National Alcoholism, with former Senator Hughes who overcame his alcoholism

Major medical advances against alcoholism have been in improved methods of detoxifying the alcoholic patient, recognizing his emotional and emotional problems, and providing sound treatment.



Group therapy methods, such as transactional analysis, have helped many alcoholics accept responsibility for themselves and build real self-esteem—an important factor in relieving emotional pressures.



Rehabilitation has sometimes required learning a new way of making a living as this man is doing at a treatment center.

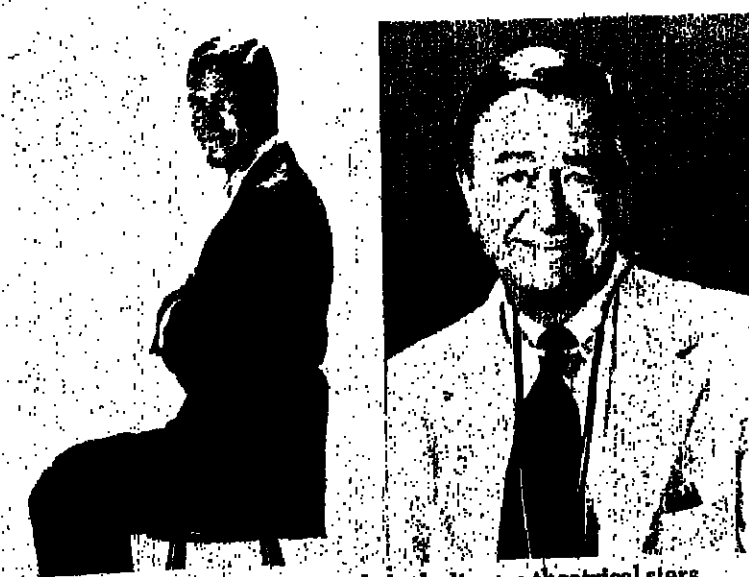


Recent scientific studies of inebriated baboons by Dr. Charles S. Lieber of Bronx VA Hospital in New York have demonstrated alcohol causes the fatty liver found in 90% of alcoholics, then develops into hepatitis and cirrhosis. Normal liver is shown on top, fatty liver after heavy alcohol consumption. Other studies are examining damage to brain and other organs as well as psychological stress contributing to alcoholism.



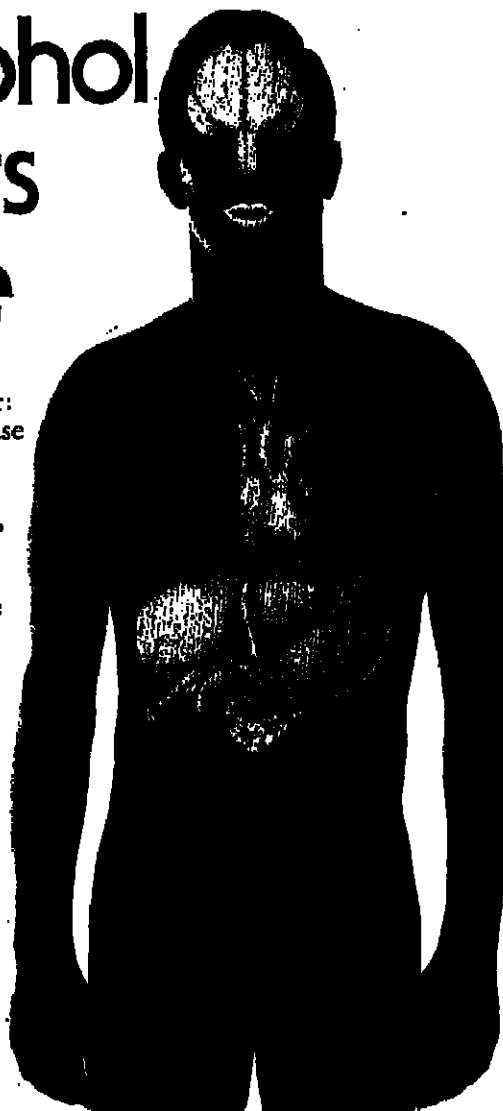
Family attitudes toward the use of alcohol play an important role in prevention of alcoholism, according to studies by National Institute on Alcohol Abuse and Alcoholism. In cultures such as that of Italy, where alcohol is taken in form of wine with food, as part of meal, the rate of alcoholism is relatively low.

Two whose alcoholism was too far advanced to be helped were Welsh poet Dylan Thomas (below, left), who was unusually gifted, and F. Scott Fitzgerald (below, right), author of *The Great Gatsby*. Both died young.



Two of the best known recovered alcoholics are theatrical stars, comedian Dick Van Dyke, and Robert Young, who achieved his greatest fame as "Marcus Welby, M.D." They revealed their recovery as a means of helping others recover.

How alcohol does its damage



IF HE'D ONLY QUIT DRINKING... OR: "If only she'd quit..." That phrase—that wish—has been uttered in despair by countless thousands of mothers, wives, husbands, children, employers, sweethearts, friends.

Today there is less and less need for despair. Alcoholism has become treatable—and preventable.

If you are going to drink, if you are going to deal with people who drink, you need to understand some of the basic facts about how alcohol works. Even if you do not drink, knowing these facts will help you understand how alcoholism can be treated.

When we swallow alcohol, a certain amount of it goes into the bloodstream, right from the stomach. It reaches the brain almost immediately and there it exerts most of its effects. In high doses it acts like an anesthetic agent—and recent studies have shown that it may induce up to a 30 per cent decrease in oxygen consumption by the brain.

The speed of alcohol passing into the brain—is very important in how the alcohol affects a person's behavior and reactions. The bigger the rush, the greater alcohol's effect.

Depression, not stimulation

The effect is to depress (not stimulate, as many people think) the brain's function. With the brain's oxygen consumption cut, the ability to perceive and judge is curtailed. The greater the concentration of alcohol in the brain, the greater the loss of sensibility and judgment. A person who is intoxicated becomes sluggish and erratic in his responses. He may appear sedated—and may actually black out. Impotency may temporarily develop, something that Shakespeare noted in *Macbeth* when he wrote that alcohol increases sexual desire but interferes with sexual performance. This tremendous impact of alcohol on the central nervous system, blocking and distorting feeling, is why years ago alcohol was used as an anesthetic to control pain in operations.

If you were in a high altitude plane and its air pressure system decompressed, an oxygen mask would drop automatically in front of your face to provide oxygen. That's because a prolonged loss of oxygen can damage the brain; loss of oxygen for only a few minutes can cause mental retardation.

In a way, the problem of alcoholism is similar. We can prevent the problem by means of a system and we need ways to intervene if danger arises.

How can we apply our knowledge of how alcohol acts on the brain? One way which all of us can use is to make sure that there is food in the stomach—especially meat or fat products—if

quickly, which does not permit them to absorb needed nutritional elements into the bloodstream.

Since some of the most serious complications of heavy drinking are at least related—if not caused—by nutritional deficiencies, added doses of vitamins should be part of the dietary intake of people who drink more than they should. Such people also are prone to colds and infectious diseases because heavy drinking causes other problems that put a great strain on the physiological makeup of their bodies. Their sleep, for example, tends to be poor, intermittent and restless in the real sense of that word. The alcohol concentrations in their brain may cause them to overestimate their abilities and their efforts may exhaust their physical and nervous strength. People who have had too much to drink often cry, "I'm exhausted..." And they are.

As a result of this exhausted state, some physicians may suggest high doses of vitamin C as both a protective and treatment approach to ward off minor but common respiratory infections. But bacterial infections must be treated with antibiotics. B-vitamins, essential for nervous tissue, may also be needed.

Alcoholics do recover

It is important for everyone—not just those who use alcohol to excess—to realize that recent Government studies confirm that over 70 per cent of alcoholic patients do get better, are able to lead useful, productive lives and avoid the physical and social complication of alcoholism.

One of the ways in which alcohol does its damage is that it sets up a vicious cycle. A man or woman may drink to excess without being aware of why he or she is doing it. It may seem like an accident. They may blow a week's pay or the family budget on a binge—and then feel so blue, guilty and despairing that the only thing that provides some relief is another drink. This process, because the basic problem of why someone is drinking to excess is not dealt with, creates our chronic alcoholics.

Therefore, it is essential that we try to understand when an individual "hurts"—and provide treatment for those hurts. Such hurts include depression, anxieties and tension, insecurities and fears, problems at home and on the job, changing life situations. It is by not paying attention to these hurts that we somehow allow alcohol to become alcoholism and do its damage.

Relationship between cancer at various sites and the use of alcohol and tobacco

Site	Number of Cases	Relationship with Use of Alcohol	Relationship with Use of Tobacco	Sex Ratio (M:F)
Hypopharynx	4,225	very strong	very strong	28.0
Larynx	5,824	very strong	very strong	27.4
Esophagus	5,007	very strong	strong	18.8
Lung	4,818	strong	very strong	11.8
Oropharynx	3,218	strong	very strong	11.8
Tongue	4,858	very strong	strong	8.3
Oral cavity (other sites)	4,145	strong	very strong	8.6
Lips	3,809	strong	strong	8.1
Bladder and other urinary organs	992		strong	2.6

Source: Hignett, et al., J. Natl. Cancer Inst. 52:1909, 1964.

Today we know that we can interrupt this vicious cycle by the judicious use of good drugs that help us relieve depression and anxieties and tensions and gain time to reorganize defenses against interlocking pressures—social, emotional, family, work and financial pressures. We must never think that just by taking a pill we create the depth of order back into a person's life that is necessary for good functioning. That will require changes on many levels and in many ways.

Your questions on alcoholism answered

Continued from page 15

Against the use of alcohol. Alcohol—for those who choose to drink in moderation—can be an adjunct to food, socializing, and sharing with other people in a beneficial way. The Secretary of the Government's Department of Health, Education, and Welfare, in a report to the Congress on Alcohol and Health, stated that there was no evidence that the moderate use of alcohol was harmful to health. The report contained certain evidence where alcohol could be shown to be of benefit to persons who choose to drink moderately.

What can be done about a hangover?

The best approach to doing something about a hangover is to prevent it. This is accomplished by being moderate, and when drinking, doing so sensibly with food in the stomach, sipping not gulping the alcohol, in relaxed, comfortable surroundings, paying attention to how the alcohol is affecting you each time you take it, not drinking when you are physically ill or emotionally upset. Some people prescribe the "hair of the dog" treatment for hangover, which is taking alcohol to ward off the unpleasant feelings of a hangover. All this does is delay the time when you will feel terrible.

Once you have a hangover, rest in a dark, quiet room. Time is the best treatment. Above all, don't try "the hair of the dog that bit you"—that leads to a hangover-drinking cycle.

What is moderate drinking?

According to a Government report, moderate drinking is no more than three one-ounce shots of hard liquor diluted or four eight-ounce glasses of beer or a half a bottle of table wine per day. This is the upper limit of safe drinking and is neither a recommendation nor a recipe to achieve. Drunkenness is a drug overdose and should always be avoided.

A word of caution about what is moderate. Some people have serious alcoholism with small doses of alcohol. I know a man who from his first few sips of a drink shows signs of drunkenness. He never takes more than two drinks in a day, but he is stone drunk on these two and is "alcoholic." What is considered moderate for some people will cause drunkenness or alcohol problems in others. The diagnosis of alcoholism does not depend on how much you drink, but what alcohol does to you.

What your doctor can do to help

A doctor's help for your alcohol problems is usually multi-staged.

Above all, doctors try to control emotions which lead to alcoholism. As in all medicine or life generally, an ounce of prevention is worth a pound of cure. However, when alcohol problems already exist, he usually prescribes a two-step program.

First, he treats the acute alcoholic and the withdrawal symptoms of heavy drinking ends.

Second, he considers long-range approaches together with the proper medication for the treatment and rehabilitation of chronic alcohol problems.

The first stage of treating an alcohol problem often requires use of modern medications that make it easy and safe to withdraw from a long bout with alcohol. The doctor will decide who will be withdrawn and watched at a hospital bed to be treated. The doctor or a responsible family member will be advised as to diagnosis and treatment.

Examination and evaluation will be emotional and social factors. It is important to define which of the different causes may have contributed to alcohol problem—how much physical, emotional pain, whether depression, loneliness, anxiety or tension; experience or absence of neurosis or psychosis, or if job or family difficulties may play a role. Adjustment in life patterns may be recommended or the suggestion may be

made that some of these problems may be better handled with psychological counseling. Medications may be prescribed as part of total therapy either to control psychic discomforts or correct nutritional deficits.

If depression is an important component, a prescription for an antidepressant can lighten the gloom, normalize reactions to disturbing stimuli while enabling the patient to function more effectively while gaining a better physical state. Such treatment may take weeks; it provides the best benefits after months. As depression lifts, patients report less guilt feelings, less despair, less desire for alcohol.

When anxiety and tension are an important component with or without depressions, these can be controlled. If they are related to severe emotional disturbance there are specific medications for major psychic disorders. For less severe disturbances there are minor tranquilizers.

Principle of medication

Some patients can be helped by deterrent drugs, such as disulfiram (Antabuse). Such drugs make the patients uncomfortably sick when they take alcohol. The experience is so unpleasant that the person tends to avoid the combination of the anti-alcohol drug and alcohol. Of course, one can bring a patient to medicine but that does not necessarily assure that medicine will be taken. In regard to any or all medicinal drugs used in alcoholism there are a few simple principles.

What you can do to help yourself

Alcoholics—nonalcoholic and alcoholic—can do a great deal to help their doctor. Don't wait for him to ask questions about your alcohol problems, being any alcohol problem. Inform him promptly to his attention at the first sign. Be sure you freely and fully inform him whether you drink at all and you report every time you drink what your status is in respect to alcohol intake. Tell him frankly about the situation, about the pressures of work, relatives, children, or other anxieties which you can identify contributing to the alcohol problem.

It is important, not only for the prevention or treatment of a drinking problem but also to help keep you in the best of health. Your use of alcohol may interfere with medications your doctor may be prescribing for you. It may willfully or seriously alter the effects of other medicines or treatments. It may be interfering with your nutrition, affecting your functioning. Your use of alcohol can influence the course of infections, of certain

chronic diseases, such as diabetes, peptic ulcer, and even allergies.

As your doctor establishes a treatment regimen, you must participate fully. A good diet, eating well but with moderation, is essential; work regularly, with moderation; play regularly (hobbies, theatre, social life) with moderation; and exercise, with moderation—all a part of regular living.

What the family can do to help

"If he or she only wanted to, they'd stop drinking" is the kind of thinking too many of us have about alcoholic people. Yet the family can be the most important ingredient in recovery. Alcoholics Anonymous proved that forty years ago when a "family" of fellow-sufferers joined together to help each other. It was proved moreover by the success of A1-Anon, made up of spouses of alcoholics, and by A1-Teen, made up of children of alcoholics. It has helped many families.

No one wants to be an alcoholic. To simply tell an alcoholic, to stop drinking, is not unlike telling a person with



Hospitals, which once rejected alcoholic patients, now detoxify them.

The medicine is chosen first to—if possible—remove the pressure causing the desire to drink or reduce the impulsiveness which is common to people with drinking problems. If anger can be restrained or deferred, frustration minimized, both patient and the therapist have time to head off an alcoholic bout. Relapses into drinking are all too often an impulsive reaction to stress.

Two things must always be remembered: Don't mix drinking with drugs. Don't mix drinking with driving.

Both the patient and the family must be involved in the treatment and rehabilitation program. Patients with alcoholism come to the doctor looking for medicine to cure them or for something to help them drink moderately. Since alcoholism requires a different kind of treatment, it is important to have the individual patient part of the treatment planning process since the "Do as I say" approach may not be

helpful in alcoholism. Studies confirm that programs which involve the patient in treatment decisions can be successful as well as rewarding.

In the second stage, besides prescribing medicines that are individualized for the patient's needs, the doctor will also be familiar with all of the treatment facilities in the community to help the patient and the family get the necessary counseling and support to help in recovery. Of course at all times, medication will be taken to make sure that the physical complications common to alcoholism are found, treated and corrected. Patient and family must always remember that alcoholism does not develop in isolation. Specialists treating alcoholic people will tell you that talking to the spouse about his or her behavior will help the alcoholic make recovery.

Where the treatment is individualized, success rates are high.

pneumonia to stop coughing. Instead of criticizing and finding fault (and who can blame anyone for wanting to), urge the person for whom you care to get some help for his sickness. Offer to accompany him to the doctor, help him talk to the doctor about a subject that has been taboo for too many



people for too long. Offer to get help yourself if the doctor finds that you may be one contributory factor to the illness. Bring it out in the open. Do not be afraid to discuss the illness of alcoholism with the children while the alcoholic parent is present. The best hope for all is to break the conspiracy of silence and destroy the stigma that need not exist. Although you may have to draw the line about things you will and will not put up with (and once you've set a limit and clearly communicated it, then stick by it), you need to understand that slips along the road to recovery are not uncommon. You should be there to help the alcoholic person pick up the pieces and begin again. But together with the doctor or counselor, try to learn what caused the slip so that it will have less likelihood of happening again. Compassion and caring and understanding go a long way in helping any of us recover from any illness.

We must remember that there is a secret conspiracy around alcoholism. The patient and those around him try not to notice the serious progress of the alcoholic, and the more severe the alcoholic, the more secretive we become. The reason: we mistakenly believe that the alcoholic is morally weak, not ill. Yet we cannot ignore a serious, treatable illness in those we care about.

Depression, anxiety and alcohol

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he can do to alter this pattern. He may need psychotherapy. He may need spiritual help. He may need new friends who will help him control his drinking; this is what Alcoholics Anonymous does for many who have suffered badly from alcoholism. The anti-depressant drugs can help alleviate the distortion created by his depressed feelings, gaining time for him to find new ways to live with satisfaction.

Anxiety, tension and alcohol

People also use alcohol to try to cope with other inner pressures.

For example, the anxieties and tensions that plague society today are among the commonest factors contributing to the addictive use of alcohol. Uncertainty and insecurity, fears—real and imagined—feelings of inadequacy or real deficiencies, unfulfilled goals and excessive ambitions, all combine to create what some have called The Age of Anxiety.

Some of these anxieties and tensions occur with a particular intensity and frequency at certain periods of life. For example, in adolescence the insecurities of immaturity play an enormous role. The adolescent is often physically full-grown but emotionally he is not. He may be terrified at what will soon be expected of him as an adult. This is one of the peak periods



for the excessive use of alcohol—with both boys and girls trying to bolster their confidence with it while simultaneously coping with their scholastic problems, their sexual feelings and desires to be attractive, popular, and "grown-up." Both sexes try to look "grown-up" by cigarette smoking. All these pressures of growing up create a situation in the teenage period that makes the use of alcohol and cigarettes a common pattern. The use of alcohol at this time may become a lifelong way of handling stresses.

Later, for both men and women, the

stresses of marital situations during their 20s and 30s may contribute to feelings of tension and anxiety that prompt a turning to alcohol. For the unmarried, fear of loneliness feeds other sources of anxiety and tension, contributing in many cases to secret drinking. In the case of many women, the growing up of their children and their departure from the home, with the change of life and life changes, or when dreams of fulfillment and achievement are not realized, may subject them to periods of anxiety, tension or depression.

When the causes of alcoholism are so complex, the remedies are equally complicated.

Early medical and psychological counseling can offer simple, preventive help. It can reduce anxieties about children and their behavior. As in the case of the drug treatment of depressions, there are a wide range of medicines such as the minor tranquilizers which, in conjunction with other measures, may help to reduce excessive anxieties, tensions and disabling attitudes and habits which contribute to the interlocking pressures pushing vulnerable people to drink.

Severe disturbances and blackouts

People experiencing severe psychiatric disturbances may resort to alcohol to ease their painful inner chaos. In such cases, the major tranquilizers, although not specific for alcoholism, can play an important although adjunctive role in controlling an underlying emotional disorganization or disturbance known to physicians as a psychosis. Here again, the easing of the burden of the psychological disturbance can

permit other treatment methods to be brought into play, heading off the complications arising from alcoholism. In some people, problems with alcohol occur because they are trying to conceal from themselves feelings they reject and would rather not face. For some these feelings of rage, jealousy, mistrust, suspicion and hatred are so intense that they have "black-outs" while drinking—a severe manifestation of alcoholism.

Reality of alcoholism

One of the most serious forms of alcoholic problems occurs in those people who need to drink so that they are really knocked out of this world. These people must maintain that state of oblivion—and such drinkers are the ones who most frequently develop liver disease, gastrointestinal complications, nerve damage and brain impairment. Their diet and nutritional status is poor. They are seriously ill. Although they are a relatively small portion of the total alcoholic population of this country, their numbers are too large as every city's Skid Row attests.

One of the unfortunate aspects of their drinking is that most people believe that the Skid Row alcoholic is "the" alcoholic—whereas in reality alcoholics are shakily holding down jobs, reasonably well-dressed, living with a family, struggling with depression and tension and anxiety—and suffering in secret, trying to get out of his or her drinking. Skid Row is reality, but it is only the end of a long road that need not be traveled.

There are other serious complications of alcohol problems, but these are the major ones, and most are treatable.

Wednesday, April 14, 1976

Anti-Pregnancy Vaccine Undergoing Clinical Tests

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the conjugate has also been administered there to a small number of sterilized volunteers—women of child-bearing age and proven fertility prior to tubal ligation.

Details of their findings, which show long-lasting yet reversible antibody response to the vaccine, are described in *Contraception* (Feb., 1976).

Although the Indian scientists caution that much more research will be necessary to establish the vaccine's efficacy and ultimate safety, they believe evidence accumulated so far indicates the feasibility of this approach to the problem of fertility control. Animal tests have been negative for toxicity, the report states, and human subjects have shown no adverse reactions.

Antibodies Produced

Injection of the vaccine in the women was followed within six to eight weeks by production of antibodies capable of reacting immunologically with the complete HCG molecule and at the

same time neutralizing its biologic activity, the investigators found. Additionally, immunization elicited the formation of antitetanus antibodies, a dividend of importance in many parts of the world.

The major problem faced by the investigators in developing a vaccine against HCG was the fact that the alpha-subunit of this hormone is "largely identical" to the alpha-subunit of three other hormones: thyroid-stimulating hormone, follicle-stimulating hormone, and luteinizing hormone.

The team thus turned to the beta-subunit and succeeded—by use of immunosorption techniques—in producing a purified "processed" preparation that has little or no cross-reactivity with other hormones.

In the limited clinical studies reported by the All India research group, four young women who were sterilized after completing their families received four injections of the vaccine during a period of about a month. All demonstrated a positive response, with pro-

Onset Age Misconcepts Cloud Diagnoses of Cystic Fibrosis

By THOMAS BULGER

Special Tribune Correspondent

VANCOUVER, B.C.—Although the symptoms of cystic fibrosis classically appear in early infancy, it is insufficiently appreciated that they may more rarely appear for the first time in late adolescence or early adulthood, according to a Canadian investigator.

The misconceptions that an adult is "too old" or a child is "too well" to have the disease may cause physicians to miss an important diagnosis, says Dr. Anthony J. Nolan of the Royal Columbian Hospital chest service.

Dr. Nolan reported on three patients who first came to medical attention because of respiratory problems at ages 19, 20, and 26, and who were eventually found to have cystic fibrosis despite the lack of clearly related symptoms in childhood.

Respiratory Infections

Each patient had a respiratory tract infection with *Staphylococcus aureus* at presentation, and two had *Pseudomonas* infections as well—both very typical of cystic fibrosis. All three had radiological evidence of acute and chronic sinusitis. Two of the three had also previously had mild abdominal complaints thought in retrospect to be suggestive of impaired pancreatic function, but these had never been sufficiently serious to cause either to consult a physician.

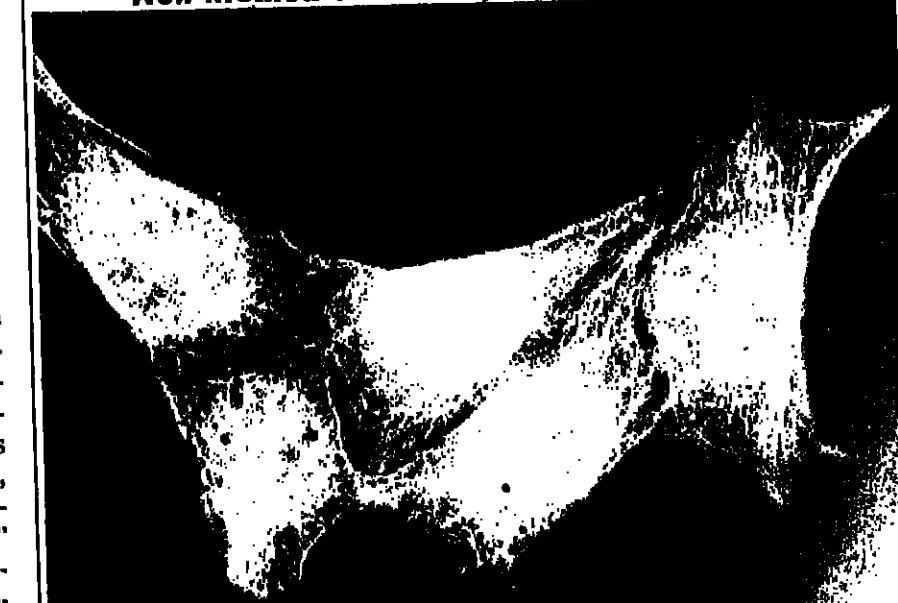
Significantly, all three had a family history of pulmonary disease, but no history of cystic fibrosis. One patient's brother had died at age 18 of bronchiectasis; a second patient had a family history of "asthma," a non-smoking grandfather with chronic bronchitis, and a four-year-old sister with recurrent lung infections; and the third patient had a grandmother with a lifelong productive cough, finally dying at age 50 with a diagnosis of tuberculosis.

"Therefore," Dr. Nolan said, "the combination of a suggestive family history in a patient with respiratory symptoms, especially when there is susceptibility to infections with *Staphylococcus aureus* or *Pseudomonas aeruginosa*, should prompt the physician to investigate the level of sweat electrolytes," and consider cystic fibrosis if high sodium chloride levels are found in exocrine secretions. "A history of abdominal problems, a suggestive childhood history, or a family history of cystic fibrosis are not necessary for the diagnosis."

Dr. Nolan stressed the importance of differentiating the adult patient with cystic fibrosis, a predominantly genetic disease from the patient with respiratory disease due mainly to environmental causes. Among the reasons he listed:

- Failure to realize that a patient has cystic fibrosis may result in the treatment of his respiratory infections with inappropriate antibiotics. As mentioned, respiratory infections in such a patient are frequently caused by *Staphylococcus aureus* or *Pseudomonas*, and the latter is found more frequently after inappropriate antibiotic therapy.
- The complications of cystic fibrosis can be anticipated and sometimes prevented—or treated most appropriately if prevention should fail—only if the underlying disease process is identified. For example, consideration of resective surgery for pulmonary complications, or laparotomy for apparent intestinal obstruction, may be considerably modified when the true nature of the disorder is recognized.
- The diagnosis of cystic fibrosis has important implications for the patient's reproductive life. While reports have appeared of males with the disease bearing fertile, the overwhelming majority are not. Females are often capable of child bearing, but suffer a much higher incidence of obstetric complications.

New Method of Identifying Cancer Cells



New immunofluorescent staining process which brings out structural abnormalities in malignant cells above may replace electron microscopy as diagnostic tool. Developed by Dr. B. R. Brinkley and colleagues at U. of Texas Medical Branch, Galveston, technique utilizes an antibody probe.

Axial Tomography Sifts Hematoma From Cerebral Infarction in Stroke

By SHERRY BENN
Special Tribune Correspondent

DALLAS—Computerized axial tomography (CAT) is the most accurate means of differentiating intracerebral hemorrhage from infarction in stroke patients, according to Dr. J. K. Campbell, consultant neurologist at the Mayo Clinic.

He told the Joint Meeting on Stroke and Cerebral Circulation here that the diagnostic accuracy possible with CAT makes it more reliable than previously used techniques.

Whereas an arteriogram may show an avascular area and an isotope scan may indicate no abnormality or simply an area of increased uptake, the CAT shows the morphology of the lesion quite clearly, Dr. Campbell said.

"One can see whether it has ruptured into the ventricular system," he added, "and be absolutely certain it is a hematoma."

In case of infarction, CAT will show whether the normal morphology of the brain is being deformed. But most important, said Dr. Campbell, is the fact that the technique can show when a

bodies had been detected in her milk.

Tests were made to determine whether sufficient circulating antibodies would be present over fairly long periods of time to bind with the amounts of HCG that could be expected from an implanting blastocyst. Therefore, a volunteer who had been immunized about 11 months previously was given two separate injections of HCG (totaling 6,000 I.U.) within 24 hours.

The results showed, the investigators report, that the anti-HCG titers fell promptly but remained above zero and began rising 36 hours after the initial dose. The starting level was reached 21 days following that first HCG injection, yet no further increase was seen—a finding that suggests, in the research team's opinion, that HCG alone does not act as a booster in women immunized with the conjugate. F.G.

clinical diagnosis of cerebral infarction is wrong.

In his study at the Mayo Clinic, Dr. Campbell and his colleagues are trying to define the whole spectrum of change in cerebral infarction by scanning patients at different stages after their infarcts.

"Generally, it is not practical to follow a single patient's progress for several weeks from the time of his infarction," he said, "because one is loathe to expose him to multiple irradiation and to keep him in the hospital for an inordinate length of time."

However, a small pilot study is going on at the Mayo Clinic now, with a group of patients who volunteered to be scanned repeatedly after their strokes. Every other day for a few days, then every week for a month, computerized tomograms are done on these patients. Then they are followed at monthly intervals up to six months. The aim of the study is to assess the morphologic evolution and resolution of the infarct or the cerebral hematoma, Dr. Campbell said.

Why use a drug to fight a drug problem

SCIENTIFIC STUDIES over many years have shown that it is rare for alcoholism to be caused by any one factor. Instead a number of interlocking factors—psychological and emotional, social and economic—are usually intertwined in the individual's background and present situation in such a way that their pressures reinforce the need to find relief in drinking. In each case the strength of those factors is different.

Working with patients who suffered from alcoholism, doctors found that many of them wanted to be treated. They were eager for a "magic bullet" to relieve them of the need to drink.

Breaking up pressures

However, there is no "magic bullet" for alcoholism. What has been found is that if the interlocking relationship of pressure factors pushing a person into drinking can be disrupted, the pattern of excessive drinking can be halted. Then, with additional help to cope with other factors that are troubling the individual, the total pattern can be broken and a pattern of sobriety developed.

One of the first drugs found to be helpful in combating alcoholism simply makes the person who takes it extremely ill if he takes a drink. It is a drug that causes a swift and violent reaction to alcohol. When this drug, which is known as Antabuse, first was introduced it was thought it would promptly reduce the number of people who suffer from alcoholism. However, its reaction is so extreme that trying to use it with all people who have an alcohol problem hasn't worked well. Only certain types of patients benefit from it. But with certain selected patients with severe chronic alcoholism who need a kind of chemical fence to keep them from taking a drink, it has helped to keep them sober until they can get some positive benefits from other types of therapy.

In breaking up the interlocking factors that underlie most alcoholism, other modern drugs have been found to be effective. Some of these drugs, the tranquilizers, have been found to reduce the nervous anxiety of many suffering from alcoholism. The anxiety may arise from their work, their uneasiness in social situations or their sex-

ual life or some change in their life situation. If the anxiety can be relieved, the pressure to drink is reduced to the point where it can be further reduced by other forms of aid. One of the difficulties in dealing with the alcoholic individual is that his behavior arouses criticism—which intensifies his anxiety. He may drink more and then defend his drinking more ardently. If the anxiety can be reduced, he no longer has to "cling to the bottle," and he can accept other help, take satisfaction in his accomplishments. Another aspect of this is the fact that simply giving up his alcohol—his refuge—makes him anxious and tense.

In the same way, antidepressant drugs may break up the interlocking pattern that makes everything look so hopeless to the depressed person.

Gaining time for help

The problem is to use these modern drugs temporarily to gain time to reorganize defenses against the interlocking pressures in the life of the individual suffering from alcoholism. He may need counseling, he and his wife may need family therapy, he may need psychotherapy, he may need a job—which he couldn't get because job interviews made him so nervous that he drank—and didn't get the job.

However, no one should use tranquilizers or antidepressants on his own—especially in conjunction with alcohol. The patient who is struggling

with alcoholism is sick enough to require the care of a physician so that total treatment—not just medication—can be used to help him safely and scientifically. No doctor should prescribe a tranquilizer unless he knows how much alcohol the patient has had.

Attitudes aiding sobriety

There is, we'll say again, no "magic bullet" for alcoholism. But the interlocking factors that cause alcoholism can be broken up—and the patient can be helped to develop attitudes that help him stay sober.

The practice of medicine is directed toward helping people function better and hurt less. Many times this means that the doctor offers a substitute for what is missing. In diabetes, he may prescribe insulin even though he knows it will require a lifetime use. In alcoholism, he may prescribe a drug that alleviates feelings of anxiety, depression, or tension. However, these are temporary aids.

Modern prescription antidepressant drugs, properly used under a doctor's supervision, are not addiction-producing. Most of the minor tranquilizers used by physicians do not have even a tiny fraction of the habituating action of alcohol or tobacco. Prescribed antidepressants and tranquilizers do not depressants and tranquilizers do not damage liver or heart, are free from the serious effects on the brain or the long-term use of alcohol or tobacco.

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Indications: Infections due to susceptible strains of the following gram-negative organisms: *H. influenzae*, *E. coli*, *P. mirabilis* and *N. gonorrhoeae*; and gram-positive organisms: streptococci (including *Streptococcus faecalis*), *D. pneumoniae* and nonpenicillinase-producing staphylococci. Therapy may be instituted prior to obtaining results from bacteriological and susceptibility studies to determine causative organisms and susceptibility to amoxicillin.

Contraindications: In individuals with history of allergic reaction to penicillins.

WARNINGS: SERIOUS AND OCCASIONALLY FATAL HYPERSENSITIVITY (ANAPHYLACTOID) REACTIONS REPORTED IN PATIENTS ON PENICILLIN THERAPY. ALTHOUGH MORE FREQUENT FOLLOWING PARENTERAL THERAPY, ANAPHYLAXIS HAS OCCURRED IN PATIENTS ON ORAL PENICILLINS. MORE LIKELY IN INDIVIDUALS WITH HISTORY OF SENSITIVITY TO MULTIPLE ALLERGENS. BEFORE THERAPY, INQUIRE CONCERNING PREVIOUS HYPERSENSITIVITY REACTIONS TO PENICILLINS, CEPHALOSPORINS OR OTHER ALLERGENS. IF ALLERGIC REACTION OCCURS, INSTITUTE APPROPRIATE THERAPY AND CONSIDER DISCONTINUANCE OF AMOXICILLIN. SERIOUS ANAPHYLACTOID REACTIONS REQUIRE IMMEDIATE EMERGENCY TREATMENT WITH EPINEPHRINE, ADMINISTER OXYGEN, INTRAVENOUS STEROIDS AND AIRWAY MANAGEMENT, INCLUDING INTUBATION, AS INDICATED.

Usage in Pregnancy: Safety in pregnancy not established.

Precautions: As with any potent drug, assess renal, hepatic and hematopoietic function periodically during prolonged therapy. Keep in mind possibility of superinfections with mycotic or bacterial pathogens; if they occur, discontinue drug and/or institute appropriate therapy.

Adverse Reactions: As with other penicillins, untoward reactions will likely be essentially limited to sensitivity phenomena and more likely occur in individuals previously demonstrating penicillin hypersensitivity and those with history of allergy, asthma, hay fever or urticaria. Adverse reactions reported as associated with use of penicillins: *Gastrointestinal:* Nausea, vomiting, diarrhea. *Hypersensitivity Reactions:* Erythematous maculopapular rashes, urticaria. *NOTE:* Urticaria, other skin rashes and serum sickness-like reactions may be controlled with antihistamines and, if necessary, systemic corticosteroids. Discontinue amoxicillin unless condition is believed to be life-threatening and amenable only to amoxicillin therapy. *Liver:* Moderate rise in SGOT noted, but significance unknown. *Hemic and Lymphatic Systems:* Anemia, thrombocytopenia, thrombocytopenic purpura, eosinophilia, leukopenia, agranulocytosis. All are usually reversible on discontinuation of therapy and believed to be hypersensitivity phenomena.

Notes: In gonorrhea with suspected lesion of syphilis, perform dark-field examinations before amoxicillin therapy and monthly serological tests for at least four months. In chronic urinary tract infections, frequent bacteriological and clinical appraisals are necessary. Smaller than recommended doses should not be used. In stubborn infections, several weeks' therapy may be required. Except for gonorrhea, continue treatment for a minimum of 48-72 hours after patient is asymptomatic or bacterial eradication is evidenced. Treat hemolytic streptococcal infections for at least 10 days to prevent acute rheumatic fever or glomerulonephritis.

Supplied: Amoxicillin as the trihydrate: Capsules, 250 mg and 500 mg; oral suspension, 125 mg/5 ml and 250 mg/5 ml; pediatric drops, 50 mg/ml.

Roche Laboratories
Division of Hoffmann-La Roche Inc.
Nutley, New Jersey 07110

Wednesday, April 14, 1976

MEDICAL TRIBUNE

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Long-Term Beta Blocker Impressive in Arrhythmias

Medical Tribune Report

NEW ORLEANS—A newly-developed beta-adrenergic blocker has successfully controlled life-threatening arrhythmias in patients who were unresponsive to propranolol, procainamide and quinidine, a Stanford University team reported here.

The drug is acebutolol, currently available in Great Britain, but still under investigative classification in the United States.

In preliminary studies, the drug was effective in 10 of 11 patients after 30 trials with other beta-blockers had either failed to control documented ventricular arrhythmias or fibrillation, or had to be discontinued because of unacceptable side effects, according to Dr. William B. Ricks, of Stanford's Division of Cardiology. Five of the patients required one or more emergency cardioversions before acebutolol therapy was initiated, Dr. Ricks told the American College of Cardiology.

The investigator said the synthetic compound appears to be "the best of the beta blockers now available for long-term treatment of high risk cardiac patients." A major advantage of the drug is that it is well-tolerated at higher dosages than the other anti-arrhythmic compounds, he stressed.

'Unresponsive' Patients

The study series included 11 patients aged 33 to 68, with an average age of 51. All were selected for the study because they had life-threatening arrhythmias or severe ventricular arrhythmias that were "unresponsive to treatment with standard anti-arrhythmic medications given at normally accepted therapeutic doses," Dr. Ricks stated. Four had cardiomyopathy, three coronary artery disease, one mitral prolapse and three idiopathic ventricular tachycardia. Before initiation of acebutolol treatment, premature ventricular complexes

averaged 4 to 26 per minute over eight hour periods. The mean for the group was 14 PVCs per minute.

Treatment was started with 300 mg of oral acebutolol every eight hours and effectiveness was judged by the absence of symptomatic ventricular arrhythmias, as well as a decrease of 70% or more in the number of PVCs in an eight-hour period. Dosage was increased as needed at a minimum of one-week intervals.

Dr. Ricks cited as illustrative of the Stanford group's experience the case of a 68-year-old man with severe coronary artery disease and an inoperable ventricular aneurysm who had repeated episodes of VT requiring cardioversion despite treatment with procainamide and quinidine. A trial of propranolol had to be discontinued due to increased congestive failure.

"During eight months of acebutolol therapy, this patient has had no recurrence of VT requiring cardioversion and is therefore considered a treatment success. In addition, there has been a concomitant reduction in PVC frequency; however, at four months, the patient independently decreased his dosage of acebutolol and experienced a rise in PVC frequency. Upon resuming the original dosage of acebutolol, PVC suppression returned to its previous level."

Achieved Goals

In another instance, a patient with frequent asymptomatic PVCs of paroxysmal VT, documented on ambulatory ECGs prior to acebutolol therapy, "has shown a consistent and marked suppression of PVCs with no documented episodes of paroxysmal VT on monthly ambulatory ECGs."

In two instances the drug had to be discontinued because of side effects, a worsening of heart failure in one patient and the development of a lupus-

like syndrome in another. A third patient died suddenly despite PVC suppression.

Overall, Dr. Ricks reported, 10 patients achieved predefined goals for therapy. "Seven patients have now been treated successfully with acebutolol for an average of 7.7 months and, during this time, have shown no recurrence of symptomatic ventricular arrhythmias and have maintained a marked (greater than 70%) decrease in PVC frequency. There have been no significant side effects in this group," Dr. Ricks declared.

In an interview, he said the Stanford team "conceives of the drug's major value as a long-term agent in cardiac patients at high risk and in supraventricular patients with chronic obstructive lung disease. Propranolol may produce bronchospasms, but acebutolol appears to be cardioselective."

Coauthors were Drs. Donald C. Harrison and Roger A. Winkle, and Ms. Patricia Bell. N.H.

Oral Zinc Said To Ease Sickle Cell Crises

Continued from page 1

the groups will switch therapies, Dr. Prasad explained.

"We give 25 mg of elemental zinc six times a day, for a total of 150 mg," Dr. Brewer told MEDICAL TRIBUNE. "That's the same total surgeons have used for many years in wound-healing, but generally surgeons have used zinc sulfate rather than acetate, and administered it in three daily doses instead of six."

The acetate salt, he explained, causes less irritation to the stomach and intestines. "The only toxicity so far, aside from a little gastric irritation, has been copper deficiency," Dr. Brewer said. "We think that because we maintain a higher blood level of zinc there is more competition between the two metals in the intestinal absorption processes. They both compete for the same absorption sites," he noted.

"If allowed to go unchecked, copper deficiency causes a hypochromic, microcytic red cell picture and neutropenia. We avoid this by simply giving 1 mg of elemental copper daily."

Current Theory

Discussing the antisickling effect of zinc, Dr. Brewer said, "We think that all blood cells are normal when first released from the bone marrow, but because of the sickle-cell patient's abnormal hemoglobin, some of these are gradually damaged through loss of oxygen. Current theory is that calcium accumulation in the membrane is part of this damaging process, and that zinc antagonizes the process and protects the membrane from becoming irreversibly sickled."

Dr. Prasad added that calcium apparently moves inside the red cell, binds to the hemoglobin, and then to the cell membrane, making it stiff and curved. "When the process reaches the cell membrane, it becomes irreversibly sickled," he said. "However, our experience has indicated that zinc will compete with calcium. In zinc therapy, it seems to push the calcium out before the sickling process reaches the membrane."

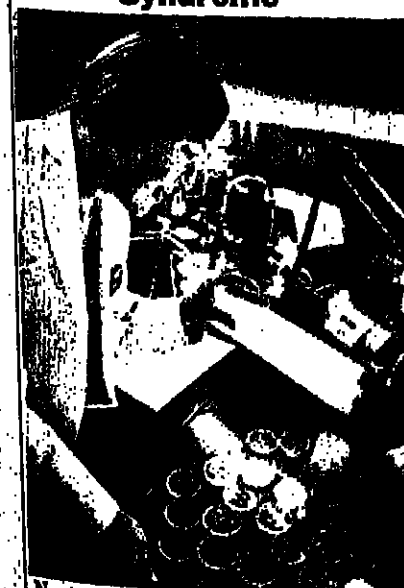
Dr. Brewer reported that zinc therapy in four out of six patients tested has produced a decrease in the number of ISCs "from a mean of 21% down to 13%." ISCs, he added, may vary from 10% to 40% of a given patient's blood cells.

In 10 patients receiving zinc for eight months to two years, "the average number of crises has been reduced from over six per year to less than

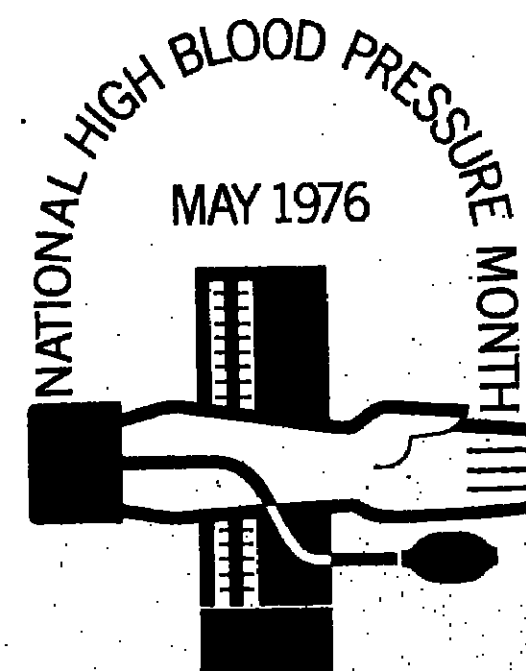
three," he declared. While the mechanism here is unknown, Dr. Prasad suggested that "the smaller vessels may get plugged off by sickled cells and therefore the tissues don't get the blood supply or oxygen they need, and this could cause the pain."

In addition to being inexpensive and easily administered, zinc is also one of the least toxic of metals that have therapeutic value, Dr. Prasad said.

Test for Sjogren's Syndrome



New antigen-antibody test for Sjogren's syndrome is performed on agar plates by Margaret Alsbaugh, Ph.D., of Scripps Clinic and Research Foundation, La Jolla, Calif. Test differentiates patients with Sjogren's syndrome from those with the syndrome plus RA.

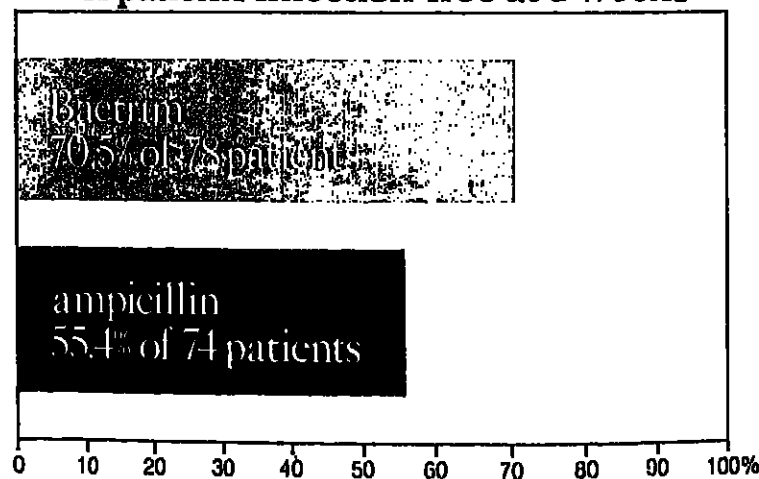


MAY 1976

In a multicenter study of patients with chronic or frequently recurrent urinary tract infections

Bactrim was 27.2% more effective than ampicillin in keeping patients infection-free for 8 weeks.*

% of patients infection-free at 8 weeks



*This percentage is arrived at by the statistical method of dividing the difference between Bactrim and ampicillin results (15.1%) by the per cent of ampicillin results (55.4%).

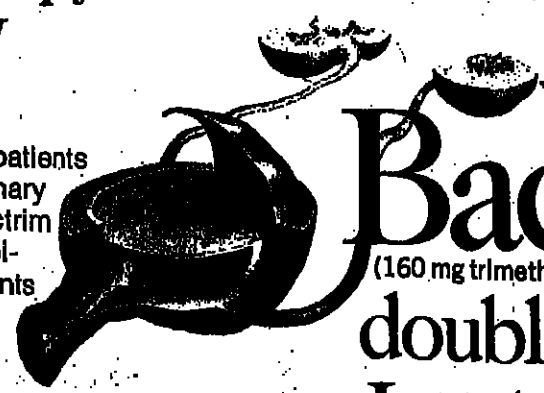
†Data on file, Hoffmann-La Roche Inc., Nutley, N.J. 07110

10-day Bactrim therapy outperforms 10-day ampicillin therapy

In a multicenter, double-blind study of patients with chronic or frequently recurrent urinary tract infection, 10-day therapy with Bactrim significantly outperformed 10-day ampicillin therapy in the percentage of patients maintaining clear cultures for 8 weeks. When compared at the end of therapy, 90.4% of 83 Bactrim-treated patients had clear cultures in contrast to 81.7% of 82 ampicillin-treated patients. Of even greater significance is the fact that a higher percentage of Bactrim-treated patients maintained clear cultures for 8 weeks. Criterion for "clear culture" was 1000 or fewer organisms/ml urine.

Adverse reactions reported in this study were relatively mild, e.g., nausea, vomiting and rash. However, more serious side effects can occur with the agents studied. Please consult the product information of each manufacturer for a complete listing of adverse reactions. Usual Bactrim therapy is 10 to 14 days. Bactrim is contraindicated during pregnancy or the nursing period. Maintain adequate fluid intake; perform frequent OBC's and urinalyses with microscopic examination. SXT sensitivity discs are available to test sensitivity to Bactrim.

Note: Bactrim single strength tablets were used in these clinical trials. However, studies have established the bioequivalency of Bactrim DS with the single strength tablets.



Bactrim DS

(160 mg trimethoprim and 800 mg sulfamethoxazole)

double strength tablets
Just 1 tablet B.I.D.

Bactrim

(80 mg trimethoprim and 400 mg sulfamethoxazole)

2 tablets B.I.D.

For chronic or frequently recurrent cystitis and pyelonephritis due to susceptible organisms.

Wednesday, April 14, 1976

MEDICAL TRIBUNE

25

One Man...and Medicine

ARTHUR M. SACKLER, M.D.
International Publisher, Medical Tribune



"The Pill"—and "The Tiger"

FOR YEARS I held out.

I could not accept the idea of continuing endocrine intervention throughout a woman's reproductive life as physiologically innocuous. The press, radio and TV hailed the "miracle" of The Pill.

I thought differently.

I had known since about 1939 that ovulation could be inhibited with the estradiol derivatives and the progestin, anhydrohydroxy progesterone. In fact, there were a few rather bold physicians who used them when patients with disabling menstrual cycles were scheduled to participate in sports events. I could not accept routine endocrine intervention for a score or more years for millions of women.

Little did I know what was to come. It took me years to grudgingly "accept" The Pill.

Accepting The Pill

I did so finally by a series of rationalizations and qualifications. Well, I said, women who have been pregnant and/or nursing a good part of their lives are subject to major endocrine shifts, the titres of ovarian hormones in pregnancy are enormous, the effect of prolactin significant. Slowly I accepted what looked like "the inevitable" but, even then, with modifications. "Okay, use The Pill—but selectively for honeymoon or vacations. If for a longer period of time, try not to exceed nine months at the most." I was trying to adjust "endocrine contraception" to other "physiological" endocrine events.

Then the headlines which hailed The Revolution of The Pill began to hail another revolution—this time The Sexual Revolution. And, revolution it has been. In fact, I even reached the point where I believed the Sexual Revolution, in contradistinction to the Generation Gap, the revolutions of youth and even most political revolutions, may have produced more permanent social changes.

And, insofar as a revolution adds to the rights of those who have been deprived and brings them a greater measure of fulfillment and satisfaction, I am no counterrevolutionary. But I should make it clear—it must add to and not reduce the individual's rights, the fulfillment and satisfaction with life, and must do so at a fair price, certainly without adding risk to life and health.

Then I began to notice how The Pill and the Sexual Revolution were negatively impacting on the actions and be-

havior of our government. Distressingly, it introduced a double standard—something unacceptable in science—in the clearance of medications for marketing. Simply check the number of oral contraceptive pill preparations put on the market in recent years and the virtual interdiction for years of new cardiovascular medications.

The possible social conditioning of government actions may go beyond the oral contraceptive drugs—it appears to include devices and appropriations for birth control research and services. Even as we must recognize the need for intrauterine devices, one does not have to accept the assumption that these are also innocuous or generally applicable. It is difficult to reconcile the continuing presence of a foreign body with freedom from potential side reactions. In this area, one wonders to what extent the advocacy of birth control propaganda has distorted realities—not only as to side effects but also as to the simplicity and virtual freedom from discomfort of inserting and removing these devices. The success of birth control propaganda is reflected also in the millions or scores of millions being spent by the U.S. government to disseminate contraceptive technologies both here and abroad.

The New Headlines

It now appears that the time has come, as it inevitably must, when reality begins to assert itself. The press and TV and women's magazines, which previously coined headline after headline on the miracle of The Pill and its liberation of women, now scream "Danger!"

"Liver Peril Linked to Long Use of Oral Birth Pills"

"Birth Control Pills May Cause Tumors, Researchers Suggest"

"Pill Called Perilous to Women Over 40"

"Report Associates Pill With Liver Cancer"

These are but a few recent headlines from three of America's major newspapers. None has questioned editorially where our government safeguards were before these pills were introduced. Our Food and Drug law required proof of safety, even before the 1962 legislative requirement of efficacy.

Now we see additional new headlines: I never advocated oral contracep-

Medicine on Stamps

Robert Barany



Born in Vienna, Robert Barany (1876-1936) received his M.D. from the University of Vienna, then joined the staff of the Vienna Ear Clinic. His many accomplishments, which led to a Nobel Prize in 1914, include the Barany tests of semicircular canal function and the "Barany Syndrome" (vertigo, occipital pain, and unilateral deafness).

Text: Dr. Joseph Kler
Stamp: Minkus Publications, Inc., New York

tion; when I accepted it, I did so with qualifications. Today, however, we have less choice. We have no choice but to recognize the realities of the present. The Pill, with the help of the press, has created a true Sexual Revolution, one which radically and remarkably changed the mores of our people in many lands. The press, which in significant measure helped create that revolution, must responsibly help educate the public to contraceptive hazards—without hysteria. It is cruel to whip people from a belief in "miracles" to the dangers of "devils."

Defining Safe Use

Having wrought so great a change in our mores, we can no longer simply "turn back." Of course, hazardous oral contraceptives must be removed from the market. Efforts must be made to define the optimal way of using the safer agents. Having encouraged sexual permissiveness, it would be dangerous to deprive the public of the convenience of effective oral contraceptives—and expose it to an epidemic of unwanted pregnancies and unnecessary abortions. We must define their responsible and safest possible use.

Unhappily, women throughout the world have been encouraged to "ride the tiger" endocrinologically. It is not easy to get off safely.

Trouble from the '30s

Medical Tribune Report

BUFFALO, N.Y.—Physicians should be on the lookout for thyroid tumors, both malignant and benign, in patients who, as children, received x-ray treatments to the head and neck area, according to Dr. Katsutaro Shimaoka, of the Roswell Park Memorial Institute here. The incidence of thyroid cancer is greater than would otherwise be expected in patients who, during the 1930s and 40s, received the x-ray therapy that was often given for enlarged tonsils and adenoids, thymic enlargement, tuberculosis, asthma, ring worms, facial acne and other skin conditions, Dr. Shimaoka said.

EPIGRAMS—Clinical and Otherwise

For the world, I count it not an inn, but an hospital, and a place, not to live, but to die in.

Sir Thomas Browne
(1605-82)
Religio Medici

ROCHE
Roche Laboratories
Division of Hoffmann-La Roche Inc.
Nutley, New Jersey 07110

Surrey TW9 2LS

Tel: 081 332 2422
Fax: 081 332 0939

Tribune Economic Analysis



Casino Gambling: Answer to N.Y.'s Fiscal Problems?

BY ELIOT JANEWAY
Consulting Economist

The urgency of New York City's need to explore new money-raising channels is accentuated by two considerations. This year's massive deficit financing needs will be modest alongside next year's; and a frightening procession of major cities are lining up behind New York. Philadelphia and Detroit are the most conspicuous examples.

One alternative has just been advanced in a bold article by Pete Hamill in the *Village Voice*. The point of it is to advise New York and, presumably, other busted cities to prepare for gambling to tide them over their money troubles. Hamill is right about the direction in which bankruptcy is taking urban finance. He may not be right about the route gambling will take.

If New York is leading its sister cities far enough along the Latin American way for legalized casino gambling to be on the agenda here as it is there, it behooves American opinion to weigh the alternatives. Municipal ownership of slot machines offers a better way for cities to cash in on the gambling urge than franchising casinos.

Gambling also promises a more candid way of coping than looting the city employee pension funds and flouting scare headlines that threaten to take civil servants off Social Security.

Ask Janeway

The federal government's unemployment figures—seasonally adjusted—have me really bamboozled. Just what does "seasonally adjusted" mean? How does it affect the unemployment count?

California M.D.

"Seasonally adjusted," Lake Erie never freezes.

The purpose of seasonal adjustment is to equalize business conditions. For example, if employment is expected to drop in January, and it doesn't, the seasonal adjustment factor counts it as rising. If unemployment is expected to rise a lot in February, and it merely inches up, the seasonal adjustment reporting basis counts it as falling. Conversely, if employment is expected to rise in April, and it falls instead, the seasonal adjustment is reported as down.

Don't feel uneasy or upset about being confused by the latest seasonal adjustment figures. The statistical bureaucracy has been making the winter adjustment on the employment figures look more favorable than normal. This means that if the economy doesn't strengthen significantly by spring, the April adjustment will look more unfavorable than normal.

"Doctors and Their Financial Futures," a seminar for medical professionals, will feature Eliot Janeway, in Cincinnati, April 22. For information, write: Medical Funding Services, 1425 E. McMillan, Cincinnati, Ohio 45206.

One of the most important things about this drug is who not to prescribe it for.

The wrong drug for these patients

Patients with impaired renal function or hepatic disease.

Patients who have a history of lactic acidosis or who drink alcohol in excess.

Patients with acute complications of diabetes mellitus, or during or immediately following surgery, where insulin is indispensable.

Patients with cardiovascular collapse (shock), congestive heart failure, and after disease states associated with hypoxemia.

The right drug for the right patient

DBI-TD[®] phenformin HCl may be the right drug for the otherwise healthy, overweight, adult-onset, nonketotic diabetic who cannot be controlled by diet alone, and who does not have increased risk of lactic acidosis.

When to stop the drug

Patients should be instructed to discontinue medication and notify their physicians immediately if G.I. symptoms, hyperventilation or other acute illness should occur.



DBI-TD[®] phenformin HCl

May be the right drug for the right patient because it lowers blood sugar without raising blood insulin, and excess insulin often leads to weight gain.

For full details, please read the prescribing information summarized below.

Geigy

DBI[®] phenformin HCl Tablets of 25 mg.
DBI-TD[®] phenformin HCl Timed-Diintegration Capsules of 50 mg.

Indications: Stable, adult diabetes mellitus; sulfonylurea failures, primary and secondary; adjunct to insulin therapy of unstable diabetes mellitus.

Contraindications: Diabetes mellitus that can be regulated by diet alone; hypersensitivity to phenformin; renal disease with impaired renal function; a history of lactic acidosis; alcoholism; juvenile diabetes mellitus that is uncomplicated and well regulated on insulin; acute complications of diabetes mellitus (metabolic acidosis, coma, infection, gangrene); during or immediately after surgery where insulin is indispensable; severe hepatic disease; cardiovascular collapse (shock); after disease states associated with hypoxemia.

Warnings: Lactic Acidosis: There have been numerous reports of lactic acidosis in patients receiving phenformin. This is an often fatal metabolic acidosis, characterized by elevated lactate levels, an increased lactate-to-pyruvate ratio, and decreased blood pH. In most cases, azotemia ranging from mild to severe was present. This may have been the result of dehydration. In some patients who developed lactic acidosis, serum creatinine was later within normal limits when the patients were properly hydrated. Observe the following specific warnings:

- Impairment of renal function increases the risk of lactic acidosis. Perform renal function tests, such as serum creatinine, prior to phenformin therapy and annually thereafter. Phenformin is contraindicated in patients with impaired renal function.
- Cardiovascular collapse (shock), congestive heart failure, acute myocardial infarction, and

other conditions characterized by hypoxemia have been associated with lactic acidosis. Hypoxemia may cause prerenal azotemia. Use phenformin in patients likely to develop azotemia with caution. The presence of a metabolic acidosis in phenformin therapy may mask the early signs of lactic acidosis. Gastrointestinal disturbances such as nausea, vomiting, diarrhea, and constipation may be confused with the early signs of lactic acidosis. Lactic acidosis may be distinguished from other conditions by the presence of ketonuria and ketonemia, or not in any and must be distinguished from other conditions. Lactic acidosis is not uncommon side effect of phenformin therapy. After increase of drug dosage, hypoxemia may cause dehydration. Nausea, vomiting, diarrhea, or constipation may herald the onset of lactic acidosis. The patient to notify the physician immediately of these symptoms or signs. The tendency of each to occur. Withdraw phenformin and institute therapy if necessary. pH, blood sugar, lactate, and pyruvate.

Precautions: Starvation Ketosis: This must be differentiated from "insulin lack" ketosis and is characterized by ketonuria, in spite of relatively normal blood sugar with little or no urinary sugar. This may result from excessive phenformin therapy or insufficient carbohydrate intake. "Destabilization" of Previously Controlled Diabetic: When laboratory abnormalities or clinical illness develop, evaluate electrolytes, pH, lactate, pyruvate, and blood and urine ketones for evidence of ketosis or lactic acidosis. With either form, withdraw phenformin and institute corrective therapy. Hypoglycemia: Although hypoglycemic reactions are rare when phenformin is used alone, every precaution should be observed during the dosage adjustment period particularly when insulin or a sulfonylurea has been given in combination with phenformin. **Adverse Reactions:** Principally gastrointestinal;

unpleasant metallic taste, continuing to anorexia, nausea and, less frequently, vomiting and diarrhea. Reduce dosage at first sign of these symptoms. In case of vomiting, the drug should be immediately withdrawn. Although rare, urticaria has been reported, as have gastrointestinal symptoms such as anorexia, nausea and vomiting following excessive alcohol intake.

(B) 98-146-103-1 (2/75) 687100 C78-8

For complete details, including dosage, please see full prescribing information.

GEIGY Pharmaceuticals
Division of CIBA-GEIGY Corporation
Ardsley, New York 10502

Czech Team on High BP in Youth: Wait and See

Medical Tribune World Service

PRAGUE, CZECHOSLOVAKIA—A 20-year prospective study of hypertension in teenagers and young adults has led a Czech team to adopt a wait-and-see attitude before initiating antihypertensive therapy in this age group. The exceptions are subjects with a positive family history or evidence of disease progression.

Dr. Jiri Widimsky of the Institute of Clinical and Experimental Medicine here said the policy—which runs counter to widely held therapeutic views—stemmed from the "surprising" observations he was able to make on 73% of the original group. Of these, 35% had returned to normotensive levels spontaneously when they were re-examined 20 years later. None in the group was currently or had been on antihypertensive therapy, Dr. Widimsky said.

An additional 40% of the series still had elevated blood pressure levels, but none showed signs of left-ventricular hypertrophy or other cardiac changes not seen initially, nor did eye-grounds show evidence of deterioration.

The study series of 100 subjects was culled from a city-wide screening of high school and university students in 1952-1954. Dr. Widimsky said that hypertension was defined at the time as 170/110 mm Hg or higher. Each of the 100 subjects received a complete workup, and a total of 73 were available for the current follow-up.

Six percent of the subjects had blood pressure levels higher than they were 20 years earlier, but with no evidence of cardiac, renal or eye ground changes, Dr. Widimsky stated. Only 1 1/2% of the total group was on hypotensive therapy. Overall, the investigator said, 17% of the series showed evidence of disease progression.

Statistical analysis of the available data, he noted, suggested that: 1) an adverse prognosis was associated with a history of hypertension in both parents, or in one parent of the opposite sex to the patient; 2) the highest blood pressure levels were seen in subjects one or both of whose parents had died of cardiovascular disease before age 60; and 3) the clearly hypertensive cases at follow-up by Dr. Widimsky's criteria were also those at the upper range of measured pressures 20 years earlier.

Dr. Widimsky said that the team failed to establish a predictive correlation between hypertension and overweight, weight gain, smoking, salt intake or level of physical activity.

Camel's Hair Warning

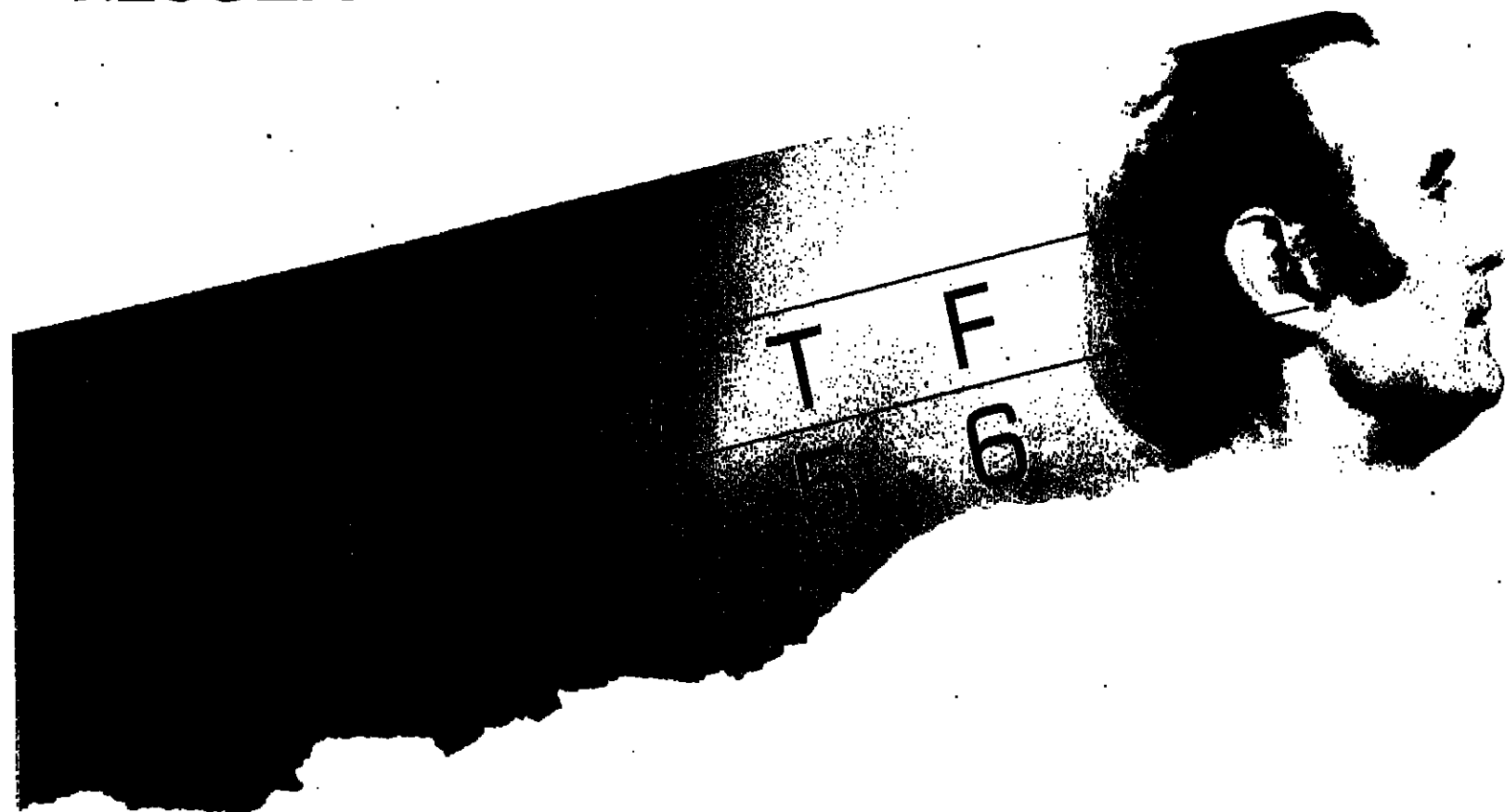
Medical Tribune Report

WASHINGTON, D.C.—The U.S. Consumer Product Safety Commission warns that hand-spun camel's hair and goat yarn recently imported from Pakistan may be contaminated with anthrax. The death from anthrax of a 31-year-old weaver in Morro Bay, Calif., prompted the investigation.

MELLARIL® (THIORIDAZINE)

TABLETS: 10 mg, 15 mg, and 25 mg thioridazine HCl, U.S.P.

IN CLINICALLY SIGNIFICANT DEPRESSIVE NEUROSIS— RESULTS OFTEN SEEN IN A WEEK



Mellaril can often help you give patients with depressive neurosis relief within a week. In 14 double-blind studies of four weeks duration, 339 patients with depressive neurosis received Mellaril. In these studies, 55% of the overall improvement was observed by the end of the first week, and a total of 293 patients (86%) improved during the four weeks.*

With Mellaril, patients often have an end to such symptoms as insomnia, G.I. symptoms, irritability, dejection, and hopelessness before they have a chance to become entrenched.

*Data on file at Sandoz Pharmaceuticals.

Mellaril (thioridazine)
short-term therapy of moderate
to marked depression with variable
degrees of anxiety in patients
with depressive neurosis

Before prescribing or administering, see Sandoz literature for full product information. The following is a brief summary:

Contraindications: Severe central nervous system depression, comatose states from any cause, hyperreflexia or hypotensive heart disease of extreme degree.

Warnings: Administer cautiously to patients who have previously exhibited hypersensitivity reaction (e.g., blood dyscrasias, jaundice) to phenothiazines. Phenothiazines are capable of potentiating central nervous system depressants (e.g., anesthetics, opiates, alcohol, etc.) as well as atropine and phosphorus insecticides; carefully consider benefit versus risk in less severe disorders. During pregnancy, administer only when the potential benefits exceed the possible risks to mother and fetus.

Precautions: There have been infrequent reports of leukopenia and/or agranulocytosis and convulsive seizures. In epileptic patients, anticonvulsant medication should also be maintained. Pigmentary retinopathy observed primarily in patients receiving larger than recommended doses, is characterized by diminution of visual acuity, brownish coloring of vision, and impairment of retinal function. The possibility of its occurrence may be reduced by retaining within recommended dosage limits. Administer cautiously to patients participating in activities requiring complete mental alertness (e.g., driving), and increase dosage gradually. Orthostatic hypotension is more common in females than in males. Do not use epinephrine in treating drug-induced hypotension since phenothiazines may induce a reversed epinephrine effect on occasion. Daily doses in excess of 300 mg. should be used only in severe neuroleptic conditions.

Adverse Reactions: Central Nervous System: Drowsiness, especially with large doses, early in treatment; infrequently, pseudoparkinsonism and other extrapyramidal symptoms; rarely, nocturnal

confusion, hyperactivity, lethargy, psychotic reactions, restlessness, and headache. **Autonomic Nervous System:** Dryness of mouth, blurred vision, constipation, nausea, vomiting, diarrhea, nasal stuffiness, and pallor. **Endocrine System:** Galactorrhea, breast engorgement, amenorrhea, inhibition of ejaculation, and peripheral edema. **Skin:** Dermatitis and skin eruptions of the urticarial type, photosensitivity. **Cardiovascular System:** ECG changes (see Cardiovascular Effects below). **Other:** Rare cases described as parotid swelling. The following reactions have occurred with phenothiazines and should be considered: **Autonomic Reactions:** Miosis, constipation, anorexia, paralytic ileus. **Cutaneous Reactions:** Erythema, exfoliative dermatitis, contact dermatitis. **Blood Dyscrasias:** Agranulocytosis, leukopenia, eosinophilia, thrombocytopenia, anemia, aplastic anemia, pancytopenia. **Allergic Reactions:** Fever, laryngeal edema, angioedema, edema, asthma. **Hepatic Toxicity:** Jaundice, biliary stasis. **Cardiovascular Effects:** Changes in terminal portion of electrocardiogram, including prolongation of Q-T interval, lowering and inversion of T-wave, and appearance of a wave tentatively identified as a T or U wave have been observed with phenothiazines, including Mellaril (thioridazine); these appear to be reversible and due to altered repolarization, not myocardial damage. While there is no evidence of a causal relationship between these changes and unexpected deaths apparently due to cardiac arrest have occurred in patients showing characteristic electrocardiographic changes while taking the drug. While proposed, periodic electrocardiograms are not regarded as predictive. Hypotension, rarely resulting in cardiac arrest. **Extrapyramidal Symptoms:** Akathisia, agitation, motor restlessness, dystonic reactions, trismus, torticollis, oculobulbar, oculogyric crises, tremor, muscular rigidity, and akinesia. **Persistent**

Tardive Dyskinesia: Persistent and sometimes irreversible tardive dyskinesia, characterized by rhythmic involuntary movements of the tongue, face, mouth, or jaw (e.g., protrusion of tongue, puffing of cheeks, puckering of mouth, chewing movements) and sometimes of extremities may occur on long-term therapy or after discontinuation of therapy, the risk being greater in elderly patients on high-dose therapy, especially females; if symptoms appear, discontinue all antipsychotic agents. Syndrome may be masked if treatment is reinstituted; dosage is increased, or antipsychotic agent is switched. Fine tremulous movements of tongue may be an early sign, and fine tremulous movements of tongue may be an early sign, and syndrome may not develop if medication is stopped at that time. **Endocrine Disturbances:** Menstrual irregularities, altered libido, gynecostasia, lactation, weight gain, edema, false positive pregnancy tests. **Urinary Disturbances:** Retention, incontinence. **Other:** Hyperpyrexia; behavioral effects suggestive of a paroxysmal reaction, including excitement, bizarre dreams, aggression of psychosis, and toxic confusional states; following long-term treatment, a peculiar skin-eye syndrome marked by progressive pigmentation of skin or conjunctiva and/or accompanied by discoloration of exposed sclera and cornea; stellate or irregular opacities of anterior lens and cornea; systemic lupus erythematosus-like syndrome. **Dosage:** Dosage must be individualized according to the degree of mental and emotional disturbance, and the smallest effective dosage should be determined for each patient. In adults with depressive neurosis the usual starting dosage is 20 mg. b.i.d. and the dosage ranges from 10 mg. b.i.d. to q.i.d. In milder cases to 60 mg. t.i.d. or q.i.d. for more severely disturbed patients; the total daily dose ranges from 20 mg. to a maximum of 240 mg. **SANDOZ PHARMACEUTICALS, EAST HANOVER, NEW JERSEY 07930**

Wednesday, April 14, 1976

MEDICAL TRIBUNE

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EPCA Reduces Inhospital Deaths From MI by 50%

Continued from page 1
EPCA in 224 patients was initiated following promising early results with the non-invasive counterpulsation procedure at Tufts-New England Medical Center, Boston, where the clinical applications of EPCA were developed by Dr. John S. Banas, Associate Professor of Medicine.

In these Boston studies, conducted by Dr. Banas, external counterpulsation in patients with chronic angina, refractory to medical treatment, resulted in improved exercise tolerance in the great majority of an early series; comparable results were observed with counterpulsation in patients with unstable angina who were being prepared for catheterization or bypass surgery and whose angina was increasing in frequency and severity.

Decision to Organize Trials

On the basis of the findings by Dr. Banas and other investigators, Dr. Amsterdam said, the decision was made to organize a collaborative national trial of EPCA in early acute myocardial infarction. The protocol called for in-hospital studies for six months to one year. The principal investigators were Drs. Joseph V. Messer, Presbyterian St. Luke's Hospital, Chicago; James W. Willerson, Parkland Hospital, Dallas; J. Michael Criley, Harbor General Hospital, Torrance, Calif.; Henry S. Loeb, Hines VA Hospital, Hines, Ill.

The study population, all with documented acute myocardial infarctions, included 108 patients treated with external counterpulsation, and 116 controls. All patients had mild left ven-

tricular failure, Killip Class 2. Dr. Amsterdam noted. Treated and control groups did not differ significantly with respect to sex, age, race, previous cardiac history, infarct location, blood pressure, heart size or drug regimens. The patients entered coronary care units within 19 hours of onset of symptoms, and the treated group received a total of four hours of EPCA within the first 24 hours of symptoms.

"The in-hospital results indicated significant differences between the treated and control groups," Dr. Amsterdam reported. "Of the 108 patients in the treated group, seven patients or 7%

died, compared with 17 patients or 15% in the control group. Recurrent chest pain occurred in 41% of the treated patients, in 59% of the controls. Cardiac failure, class 3 or 4, was observed in 6% of the treated group, 15% of the controls. A total of 89% of the treated patients had changed in clinical status at discharge to Class I, compared to 77% of the controls."

'Favorable Effect'

He concluded: "EPCA, as administered in these evaluative studies, was associated with a favorable effect on the mortality and clinical course of

patients with acute myocardial infarction."

In an interview, Dr. Amsterdam noted that while the mechanism of action of external counterpulsation is not fully understood, the beneficial effects may be due to an enhancement of collateral coronary blood flow during the early phase of myocardial infarction. He stressed, however, that this was speculative and would require extensive further studies. He also stressed that, in recommending routine use of EPCA in early myocardial infarction, it was essential to remember that the procedure is contraindicated in patients with peripheral vascular disease.

In Boston, Dr. Banas told MEDICAL TRIBUNE that coronary arteriography of some patients in the early angina studies suggested that an increase in collateral circulation may have occurred in association with the use of EPCA, but he stressed that these observations were still speculative. He also speculated that if, indeed, it increased coronary blood flow, the early use of counterpulsation could be limiting the size of the myocardial infarct, but again stressed that hard evidence is lacking.

In continuing studies at Tufts, he said, he and his colleagues "are now classifying patients by wedge pressure, measuring the hemodynamics of EPCA and doing precordial mapping."

The Nose Knows

Medical Tribune Report

WASHINGTON, D.C.—The nose knows, says Dr. Robert I. Henkin, specialist in taste and smell disorders at Georgetown University School of Medicine. Dr. Henkin points out that abnormalities in the sense of smell may be the first sign of liver disease, a metabolic disorder, hypothyroidism, a brain tumor, or a malignancy anywhere in the body.

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By teaspoon or tablet

- Readily assimilated
- Well tolerated
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for
nutritional
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deficiency
anemias

Usual Dosage: ELIXIR—1 to 3 teaspoonsful daily or as directed by physician.
TABLETS—1 tablet 3 times a day or as directed by physician.
Supplied: 12 ounce bottles of Elixir; bottles of 100 Tablets.

K Kenwood Laboratories, Inc., New Rochelle, New York 10801
developers and suppliers of Cebrol™ and Kengesin™

I·L·X B12™

Elixir—each ounce represents: Iron and Ammonium Citrate, 18 gr. • Liver Fraction 1.3 gr. • Thiamine Hydrochloride, 10 mg. • Riboflavin, 4 mg. • Nicotinamide, 20 mg. • Cyanocobalamin (Vit. B12), 20 mcg. • Alcohol 8% by volume.

Tablets—each tablet contains: Ferrous Gluconate, 5 gr. • Vitamin C, 60 mg. • Cyanocobalamin (Vit. B12), 10 mcg. • Liver Fraction 2, 2 gr. • Thiamine Hydrochloride, 2 mg. • Riboflavin, 2 mg. • Nicotinamide, 20 mg.

Cebrol®

100 mg capsules

ethaverine HCl

In cerebral ischemia:

direct vasodilation of cerebral vessels; virtually no CNS effect; rare incidence of side effects permits long-term use

In peripheral vascular disorders:

relaxes smooth muscles of larger blood vessels by direct effect unrelated to muscle innervation

For additional product information and professional samples, write on your letterhead to

K Professional Service Department
KENWOOD LABORATORIES, INC.
New Rochelle, New York 10801

Indications: For the relief of cerebral and peripheral ischemia associated with arterial spasm.

Contraindications: The use of ethaverine hydrochloride is contraindicated in the presence of complete atrioventricular dissociation.

Precautions: Use with caution in patients with glaucoma. Hepatic hypersensitivity has been reported with gastrointestinal symptoms, jaundice, eosinophilia and altered liver function tests. Discontinue drug if these occur.

The safety of ethaverine hydrochloride during pregnancy or lactation has not been established; therefore it should not be used in pregnant women or in women of childbearing age unless, in the judgment of the physician, its use is deemed essential to the welfare of the patient.

Adverse Reactions: Although occurring rarely, the reported side effects of ethaverine include nausea, abdominal distress, hypotension, anorexia, constipation or diarrhea, skin rash, malaise, drowsiness, vertigo, sweating, and headache.

Dosage and Administration: One capsule three times a day.

How Supplied: 100 mg capsules in bottles of 50 and 500.

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